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The order in this section is:—**General; Vital Statistics; Epidemiology; Maternal and Child Health; Health of Students, Nurses and Hospital Staffs; Health of Old Persons and the Chronically Ill; Chronic Cardio-Respiratory Diseases; Chronic Rheumatism; Cancer; Miscellaneous Diseases; Dental Health; Mental Health.**

GENERAL

SCOTLAND. **Report of the Department of Health for Scotland 1960.** [HADDOW, T. D., Secretary]. **Part I. Health and Welfare Services.** Cmnd. 1320. 88 pp., 7 diagrams. 1961. Edinburgh: H.M. Stationery Office. [5s.]

This is a competently written report which contains something new and interesting for almost every administrator of a health service.

It has been "a good year for the nation's health". The rate of infant mortality was 26·4 "per thousand" (75·8 in 1936–40) and the maternal mortality 0·3 (4·8 in 1936–40). The death rate from pulmonary tuberculosis was 9 per 100,000 population (male 14, female 6).

A table similar to those in reports of the Ministry of Health for England and Wales gives the cost of the National Health Service. It was £83,631,000, including Hospitals and Specialist, £53,222,000; general medical, £8,187,000; pharmaceutical, £8,667,000; local health authorities, £6,358,000. After allowing for changes in the purchasing power of money, the total cost has increased during the past 10 years by 22%: in that period the gross costs of the hospital and of the pharmaceutical services has doubled and that of the local health authorities nearly trebled.

Current Health Topics. "The hospital service is using about the same number of beds for a larger number of patients who stay for a shorter time."

At school medical examinations 64·65% of the children were found to be free from defects in 1958–59: it was 60·43 in 1948–49.

The expectation of life at 45 years of age is for males 25·7 and for females 30·2: for males this is little improvement on 30 years ago but for women it is nearly 3 years longer. The diseases contributing to the higher male death rates are lung cancer, arteriosclerotic and degenerative heart disease and bronchitis.

The regional medical officers have reviewed 300 cases under the age of 50 where the person had been unemployed for 6 months or more: in only 25 was there no physical or mental handicap; in no fewer than 108 a psychosis or a psychoneurosis was diagnosed.

A WHO table is reproduced which shows that Scotland has the highest mortality from lung cancer of the 26 countries included (males, 600·5; females, 91·2 per million population).

There are 1,863 beds occupied by tuberculosis patients compared with 4,856 in 1955.

20% of the school leavers are tuberculin positive compared with 50% in 1953.

1959 was not an "influenza year" in Scotland and there were only 6 notifications of paralytic and 26 of non-paralytic poliomyelitis.

There is a well-balanced section on immunization.

Reference is made in the chapter on "Mental Health" to Mental Health Year and to the Edinburgh Conference on this topic where the theme was "Action for Mental Health". The report describes in detail the Mental Health (Scotland) Act 1960. An important difference between Scottish and English law is that in Scotland, but not in England, endorsement by a judicial authority, the sheriff, is required for compulsory detention as well as certificates from two doctors.

Local Health Authority Services. This chapter states that there are 30% more health visitors and 18% more district nurses than in 1950: the number of home helps has nearly doubled and that of child welfare clinics has increased from 365 to 478. A diagram depicts how each pound spent is allocated between the services; care of mothers and young children took 5s. 3d.; domestic help, 3s. 7d.; home nursing, 3s. 6d.; midwifery and health visiting, 1s. 8d. each; mental health 1s. 6d.; tuberculosis, care and aftercare, 1s. 6d.; and the rest which includes vaccination and immunization, 1s. 4d.

The General Practitioner Services. There are 2,665 doctors providing as principals general practitioner services of whom 1,804 worked in partnership: there were also at the end of the year 178 ordinary, and 66 trainee, assistants. The number of dentists was 1,064; 11 fewer than the previous year but courses of treatment increased by 3·4%.

Hospital and Specialist Services. Another diagram analyses hospital costs. The largest component, nursing salaries, takes 5s. 4d. of each pound; the next is 4s. 8d. for domestic, catering and other wage-earning staff; 2s. 1d. is for medical staff making a total of 12s. 1d. for

salaries and wages; the rest, 7s. 11d., includes 1s. 10d. for food; 1s. 6d. for drugs, dressings and equipment and 10d. for administration.

Staffed beds numbered 63,647; a decrease of 213 during the year. There were 992 consultants, an increase of 32.

A major hospital building programme is being actively planned.

A scheme to provide morbidity statistics has been started which will give essential particulars about all hospital patients.

Staff. The National Health Service now employs in Scotland a staff of 76,500 of whom 5,825 are doctors, 1,300 are dentists, 33,150 nurses or midwives, 850 opticians, 2,640 other medical auxiliaries and 5,000 administrative and clerical.

An important experimental course in training of nurses provides the necessary instruction in 2 instead of 3 years.

Welfare. There has been much activity in the welfare services: most of the accommodation for the aged now being provided is in purpose-built homes though there are still about 4,000 in former poor law institutions.

Allen Daley

WALKER, J. V. **A Critical Look at the Public Health Service.** *Lancet.* 1961, June 24, 1392–3.

After referring to the anxieties expressed by many, at the time when the National Health Service was introduced, about the future of the public health service, the author states that the MOH and his staff now "hold a position almost as well established as ever—except financially" but that there may be a good deal of useless wood in it which needs to be pruned. "The challenge confronting us is hardly less than it was a century ago, though the terms of it have changed."

Occasionally the MOH is still tested by how he tackles smallpox or typhoid fever and, less frequently, poliomyelitis but "cancer, coronary thrombosis and accidents are large territories yet to be conquered" as well as mental disorders and chronic rheumatism. With the advent of the Welfare State the techniques of maternal and child welfare need to be recast. Family doctors might be encouraged to hold their own maternal and child welfare clinics; the midwife and the health visitor being present at the former and the health visitor at the latter.

Schoolchildren are much healthier than they were but there has been little change in the methods used by the school health service. The author poses the question "Has the ingrained habit of traditional usage sterilized creative thought?" He suggests that it might be better to substitute selective examination of children who appear to be in need of it for the routine examination of all and spend the time so saved in the schools.

A section on health visitors and social workers states that the health visitor does undertake "case work" and questions whether full hospital training as a nurse is any longer essential. The author points out that health visitors have lost the positions of mental welfare workers and hospital almoners and are in danger of losing geriatrics.

With regard to the MOH himself the ladder of promotion began with maternal and child welfare and school health work. New ideas are now needed and recruits from, for example, psychiatry, paediatrics, geriatrics and industrial medicine would bring in the necessary new blood.

Allen Daley

DOUGLAS, J., EDGAR, W., ATKINSON, V. H., CRAWFORD, W. E. D., MACCULLOCH, G. T. & LAVERICK, R. C. **School Medical Inspection and the Family Doctor.** *Med. Officer.* 1961, June 16, v. 105, No. 24, 351–5, 3 figs.

This paper is from the City of Bradford which was a pioneer in school medical work. It recalls the criticism that routine school medical inspection is "wasteful and unproductive".

Various modifications of the examinations at entrance to school have been tested with the aim of providing "with the assistance of the family doctors," a more comprehensive examination than the medical inspection normally affords. Family doctors in the test areas with 10 or more school entrants on their lists were invited to participate. Urine was tested as a routine. The first trial scheme started early in 1959. The physical examination was made by the family doctor at a clinic session. While this was going on the school doctor discussed with the parent the child's emotional development and progress in school. The school doctor then examined the child and afterwards the 2 doctors compared their findings and gave a summary to the parent who had been invited by a carefully prepared letter which is reproduced in the paper.

An addition provided in a second scheme was that the teacher was asked to give information on a questionnaire about the children selected by him or her as being in need of special attention: it dealt with school progress, absences and behaviour: this helped to overcome the loss of contact between the teachers and the doctors resulting from the examinations being made at clinics instead of schools.

In a third test made early in 1960 the parents were asked to complete, before the examination, a questionnaire and, as a result of all the information available, certain children were selected for special examination.

The numbers of children included in the 3 schemes were 402, 441 and 336 respectively. The third scheme was regarded as the most satisfactory. A table gives the findings in each of the 3.

As expected, the incidence of "psychological defects" found was considerably higher than in ordinary routine examinations; 13·8–16·6% compared with 1·6% but most were minor and likely to respond to advice and reassurance.

The family doctors were enthusiastic about the scheme; the school doctors found that they could do better professional work in the clinics than in the schools; 25% of the teachers liked the trial schemes, 25% preferred routine medical examinations in the schools, the remainder recognized that each scheme had its advantages and disadvantages and expressed no preference; the majority of the parents welcomed the new scheme; the administrators found the new scheme more complex and time-consuming.

Among the disadvantages of the new scheme were (a)

the taking of the medical examinations away from the schools to the clinics and (b) the creation of two groups of children; those examined jointly by the family and the school doctor and those examined by the school doctor alone.

If the new scheme were extended to the whole city each of the 200 family doctors in practice there would come within the requirement of having 10 schoolchildren on his list: that is the number needed for a session of school examination work.

The scheme has helped the family doctors to understand what the school health service is trying to do.

[These are important experiments and are an improvement on the normal American practice where the family doctor fills in the school medical schedule in his office and the parent, after paying for it, sends it to the teacher.] *Allen Daley*

PARKEN, D. S. **A Service for Deaf and Partially Deaf Children.** *Med. Officer.* 1961, June 9, v. 105, No. 23, 335–8, 3 figs. [14 refs.]

A scheme involving (1) screening tests by health visitors, (2) diagnostic tests in conjunction with the ear, nose and throat specialists, and (3) a class for partially deaf children has been in operation in Poole, Dorset, (population 90,000) since 1957.

The screening tests used were devised by Professor Ewing for very young children. It was possible to test a 10% sample of infants aged 6 months or slightly older; the testing was done by health visitors who had been given special instruction. Of the 350 infants tested 18 were referred for a specialist opinion and of them 3 were found to be deaf or partially deaf.

The next stage was to compile a register of children "at risk" and for this the help of hospital specialists, family doctors and midwives was obtained. A form, which is reprinted in the paper, records particulars of abnormal ante-natal conditions, abnormal labour, peri-natal history prematurity, postmaturity, congenital abnormality, family history of deafness, any severe illness of infancy or any suspicious indication of deafness observed by the mother. A health visitor arranged for a hearing test at a clinic whenever this seemed to be desirable.

Schoolchildren are tested by audiometricians using a sweep test at 20 decibels. Those who fail are examined either at once, or after failure at a retest, by a school doctor who selects children for the Audiology Unit which supervises all work for the deaf or suspectedly deaf. Relevant information is obtained from all available sources and the child is seen by a teacher of the deaf, a psychologist conversant with problems of the deaf as well as by the school doctor. When all the data have been gathered the child goes to the Assessment Clinic which receives patients, also, from hospitals and family doctors. Some are referred for surgical treatment, some for observation only and others for special education at school or at home.

The work of a special nursery infants class is described. It is part of an ordinary school for normal infants and was opened in 1960. An essential for success is a co-operative headmistress who is really interested in the deaf. There are 6 to 8 partially deaf children in the class and the equipment needed is set out. The children associate with hearing children when they are not receiving auditory training and thus are "gradually absorbed into the general community". There is also a day nursery which receives young deaf children and the children of deaf and dumb parents so that they can hear and learn normal speech.

In due course the children pass on to a special class in a junior school.

Transistor hearing aids are supplied when needed. The teacher of the deaf visits the homes of the children to give guidance to the parents and there are portable auditory trainers available for loan to the parents.

Developments still needed include provision for the profoundly deaf, for those of secondary school age and for adults. *Allen Daley*

PAKTER, Jean, ROSNER, H. J., JACOBZINER, H. & GREENSTEIN, Frieda. **Out-of-Wedlock Births in New York City. I. Sociologic Aspects.** *Amer. J. Pub. Health.* 1961, May, v. 51, No. 5, 683–96. **II. Medical Aspects.** *Ibid.*, June, No. 6, 846–65, 1 fig.

The 2 parts of this long paper contain the results of a very detailed study of the sociological and medical aspects of the problem of illegitimate births as it exists in New York City. In recent years this problem has steadily grown in the United States as a whole and particularly in the urban areas. In the United States in 1947 the number of out-of-wedlock births represented 3·6% of all live births and by 1958 the percentage had increased to 5%. In New York City the rate has increased from 3% in 1946 to 8% in 1959.

There is a description of the method of study in which the data obtained were analysed by the ethnic groups (1) white—excluding Puerto Ricans, (2) non-white—excluding Puerto Ricans, and (3) Puerto Ricans.

The findings of this extensive and interesting study are clearly set out under many headings. Among the sociological aspects of the problem which were considered are the characteristics and age of the unmarried mother, the pregnant girl at school, parity of the unmarried mother, the welfare services in relation to the whole problem, facilities for obstetric care, the caesarian section rate and prenatal care.

The second part of the paper on medical aspects contains much statistical and other information. The first section is on the complications of pregnancy. Later sections contain descriptions with tables of data on the percentage of out-of-wedlock births in total births by ethnic groups; live births by marital status, age of mother and ethnic group and other tables of comparison on parity, prematurity, infant mortality and maternal mortality.

There is a long discussion and summary of this interesting and informative paper.

"The problem of the unwed mother and her out-of-wedlock child is only a part of a large-scale community problem of unstable family life evidenced by the large numbers of broken homes due to desertion, separation and divorce". *M. E. Delafield*

LANOIX, J. N. Rôle et formation des ingénieurs et inspecteurs sanitaires. **[The Duties and Training of Sanitary Engineers and Sanitary Inspectors]** *Rev. d'Hyg. et de Méd. Sociale.* Paris. 1961, Mar., v. 9, No. 2, 151–75. [16 refs.]

The author deals first with the sanitary engineer. The various names applied to the members of this profession are discussed and defined. Its history and developmental phases are briefly described, the present phase being concerned with as yet unsolved industrial and nuclear fission problems. The function of the sanitary engineer varies according to the body employing him. His status is now regarded as complementary to a corresponding medical officer of health and he usually has the same remuneration. The work of WHO in regard to sanitary engineering is described. Several pages are devoted to a discussion of the training curriculum which is generally based on a professional qualification in civil engineering followed by a year of special studies leading to a higher qualification. This is preferably undertaken in an engineering school of a university which also trains doctors, so that they learn to work together. Graduates in other branches of engineering—mechanical, electrical, chemical—or of biology can also become sanitary engineers and can provide a body of knowledge essential for understanding and solving modern health problems. Short courses of instruction are valuable only for raising standards in a limited field of study. Courses leading to a Master's degree in sanitary engineering are provided in some engineering schools, and in some medical schools chemical engineers or biologists with no civil engineering background can study for a similar degree in public health. The basic subjects in the curriculum are described and a number of optional courses suggested. A doctorate in Sanitary Engineering can be obtained by qualified engineers in the United States of America after 3 years' study.

The nomenclature of the sanitary inspector is discussed and his functions in advanced and developing countries. Training varies enormously throughout the world. In the United States it is being co-ordinated and standards are being raised, a B.Sc. in sanitary science being required for promotion to the higher posts. The WHO recommendations concerning the training of sanitary inspectors are quoted, together with advice as to how they should be employed. The importance of giving them some responsibility and liberty of action is emphasized and the need for developing a team spirit in those working under a medical officer of health, by frequent meetings and work towards a common goal.

[This full discussion of the functions and training of sanitary engineers and inspectors and their subordinates cannot be summarized. Those interested in the subject will profit by reading the original.] *T. H. Davey*

REV. VENEZOLANA SANIDAD Y ASISTENCIA SOCIAL. Caracas. 1960, June & Sept., v. 25, Nos. 2/3, 3–199, illustrated. La situación actual de la salud en Venezuela. **[The Current Position of Public Health in Venezuela]**

MATERNAL AND CHILD HEALTH

LUDKIN, S. **An Investigation into Local Maternal and Perinatal Deaths.** *Med. Officer.* 1961, June 30, v. 105, No. 26, 381–4.

The areas included in this enquiry were the urban districts of Consett and Stanley in the county of Durham. Slightly more than half the births were domiciliary. Each year a report is presented to a meeting to which the general practitioners and local health authority staff are invited, and the various aspects of the infant mortality experience are studied. Post-mortem examination has become routine and in 1959 45 of the 46 perinatal deaths were examined at autopsy. 34 of the deaths occurred in hospital and 12 were in infants born at home. 12 of the 45 mothers had an history of abortion, miscarriage or perinatal death and 10 of the mothers were aged 40 and over. 13 of the infants weighed 3½ lb. or less, 17 had congenital malformations and 8 had birth injuries confirmed by post-mortem examination. An appendix gives a copy of the schedule that has been completed for each perinatal death. The author suggests that a critical examination of the facts surrounding each death may lead to prevention of deaths which at present are considered to be unavoidable. *W. J. Martin*

CHRONIC CARDIO-RESPIRATORY DISEASES

GORBATOW, O. Die Herzinfarktfrequenz in einem Material der Bevölkerung von Helsinki während der Jahre 1945–1952. **[Cardiac Infarction in Helsinki, 1945–1952]** *Acta Med. Scandinavica.* 1961, v. 169, Suppl. 364, 94 pp., 11 figs. [187 refs.]

This interesting paper contains a detailed analysis of 569 cases of myocardial infarction in patients treated at the Maria Hospital, Helsinki, in the period 1945–52. This account is preceded by an extensive review and discussion of the literature of the disease under the headings of the increase in its incidence in many lands; its mortality, age and sex distribution; and seasonal incidence. Also discussed are the published references to the influence of social class on incidence about which the observations are not in accord; the apparently undoubted hereditary factor; the question of whether tobacco and alcohol play a part in causation, about

which opinions vary; and the complex question of a dietetic factor in causation.

The purpose of the particular investigation undertaken by the author was in the first place to study the extent to which certain medical and social factors influenced the incidence of myocardial infarction. The period 1945–52 was chosen because during that time no important changes in diagnosis or treatment were introduced. Comparisons were made, however, between the observations in 1945–48 and those in 1949–52 because during the latter period the general welfare and the food supply of Finland had been almost re-established after the difficult conditions existing during 1945–48 following the war in Finland which had ended in 1944.

The yearly distribution of the 569 patients studied is given in a table in which the numbers are stated and expressed as a percentage of the total annual number of patients at the Maria Hospital. In 1945 the number of cases of myocardial infarction was 15 (0·70% of total cases in hospital) and in 1948 there were 44 cases (1·94%). After this the incidence rose rapidly from 87 cases (3·88%) in 1949 to 135 cases (6·27%) in 1952.

The numbers of cases of myocardial infarction seen at all the hospitals of Helsinki are also given together with the size of the population which increased greatly during the period of study. Much detail is given on mortality, age and sex distribution and onset of the disease by month and hour of the day.

Analysis of the 569 patients in 4 social classes the definitions of which are stated indicates the higher incidence in the higher classes.

There was evidence on enquiry that hereditary factors existed for 25% of a group of 447 infarction patients and gave a family history of coronary disease as compared with only 12·5% in a control group of 263 patients with some other disease.

Other aspects which are given careful analysis include the frequency of repeated infarctions and the number of men and women among the 569 patients in whom there was a high blood pressure. 98 of 335 men and 101 of 190 women were found to have a blood pressure of 160 mm.Hg. or more.

It was found that a larger percentage of men in the infarction series took alcohol and smoked than in a control series but the mortality of male smokers was about the same as that of non-smokers. The mortality of those who took alcohol was somewhat lower than that of abstainers but their mean age was also lower.

A description with tables is also given of the consumption of food—meat, butter and sugar—in the period of the study which shows the very great increase in the available amounts of these foods after the cessation of food rationing in 1948.

There is a long discussion and also a summary of the paper in English. *M. E. Delafield*

BRITISH J. CLIN. PRACTICE. 1961, May, v. 15, No. 5, 405–71, 23 figs. (7 coloured). [Numerous refs.] **Symposium on Chronic Bronchitis** [SMART, J., Guest Editor].

It is appropriate that the *British Journal of Clinical Practice* should carry a symposium on chronic bronchitis which has been described as the "English disease", and this symposium by authors well versed in the problems of the disease is one that will be found valuable by many people who are not directly acquainted with the considerable advances in understanding which have taken place as the result of investigations largely carried out in the United Kingdom during the past 10 years. J. SMART, who is Editor of the series, writes an article entitled *Introduction and the Clinical Aspect of Chronic Bronchitis* (pp. 405–406) in which he outlines some of the problems that are dealt with by the subsequent authors. Lynne REID in an article on *The Pathology of Chronic Bronchitis* (pp. 409–420) reviews knowledge of the physiology of mucus secretion of the bronchial tree and describes the observations which she has made of the hypertrophy of mucus glands (which may be quantitatively assessed as the ratio between measurements of the thickness of the gland and the thickness of the bronchial wall) and increase in goblet cells. These are the primary lesions in chronic bronchitis. Subsequent bacterial invasion is possible for secondary changes in the bronchi and lungs, largely of a destructive kind with extensive scarring. This leads on to a discussion of the meaning, pathology and pathogenesis of emphysema complicating bronchitis and the consequent damage to the pulmonary circulation. Animal experiments are quoted to illustrate the effect of inspired irritants in producing mucus gland hypertrophy. Finally, the correlation between the pathological observations and radiological and functional changes is discussed and there is a final note on the rare condition of pituitous catarrh (bronchorrhoea). This article is an admirable summary of Dr. Reid's pioneering work.

A short article on *Sputum in Chronic Bronchitis* (pp. 423–425) by J. R. MAY discusses bacteriological and cytological techniques of examining sputum in relation to the diagnosis of infection. He concludes that "naked eye inspection usually provides adequate information . . . and . . . bacterial examination is seldom required".

The Disorders of Function in Chronic Bronchitis (pp. 429–436) are described by L. H. CAPEL. Here the physiology of gaseous exchange in the lung and its disturbance by generalized and regional reduction of ventilation are described in order to interpret the arterial blood gas abnormalities that may be found in disabled bronchitic subjects. The main functional abnormality associated with bronchitis, obstruction of airways with a consequent increase in the work of breathing, is emphasized, and the technique of simple spirometry in diagnosing airways obstruction is described.

R. H. COOKE discusses *The Problems Associated with Chronic Bronchitis and Emphysema in General Practice* (pp. 441–442) in an article which emphasizes the need for regarding the disabled bronchitic subject in relation to his family as well as his own problems. A number of problems of domestic hygiene and of administrative arrangements which may help in the solution of these problems are recounted. J. L. LIVINGSTONE deals with *The Treatment of Chronic Bronchitis* (pp. 447–451). He defines various stages of the disease and suggests (in contradistinction to Smart's insistence that bronchitis must be treated before it becomes disabling) that serious treatment is only necessary when "simple recurrent bronchitis becomes progressive". He advises that smoking

should be forbidden but that the bedroom windows should be kept open and that a hardy open-air life should be lived; gargling is suggested at the onset of an exacerbation of bronchitis. [Many clinicians would disagree with these suggestions.] Accepted chemotherapeutic regimes are described and physiotherapy is advised only in occasional cases. Broncho-dilators and oxygen therapy are mentioned. The importance of trying to get the patient to a sunny unpolluted climate is emphasized.

G. W. HAYWARD discusses *The Cardiological Complications of Chronic Bronchitis* (pp. 453–458, 491). He emphasizes the importance of distinguishing primary bronchitis from the bronchitis that may complicate pulmonary congestion in mitral stenosis or which may be an initiating cause of heart failure in subjects with hypertensive cardiac disease. He then describes the clinical manifestations and diagnosis of chronic cor pulmonale. There is no mention of blood electrolyte and arterial blood gas measurements which are so important in making the distinction. [Some clinicians would disagree with the extremely severe prognosis which he describes in cor pulmonale. In fact a number of patients survive for a remarkably long period if the bronchial obstruction causing hypoventilation is relieved, especially in those cases, not mentioned in the article, in which anatomical emphysema has not yet developed.] The appropriate therapeutic regimes for these various kinds of cases are well described.

CO_2 Narcosis in Chronic Bronchitis is described by F. J. PRIME (pp. 461–464). The mechanism of this well known complication is here most adequately described with references to the physiological investigations which have clarified this subject. The account should be readily understood by readers with only scanty knowledge of physiology. The avoidance and treatment of the condition are briefly described. Finally J. R. BIGNALL provides a brief review of *Modern Research into the Development of Chronic Bronchitis* (pp. 467–471). He emphasizes the importance of defining the nebulous concept of chronic bronchitis which has been a necessary part of research in recent years. Information derived from mortality and morbidity statistics is briefly referred to, together with the techniques that have been used in field surveys. The clear evidence of the effects of tobacco smoking and air pollution are described. The well known relationship between social class and bronchitis remains unexplained as does the rather doubtful evidence about the effect of occupation. The conclusion is that smoking is of overwhelming importance in the early stages of the disease and the harmful effects of air pollution, leading to disability and death may be greatest in those already affected by tobacco smoking.

The discriminating reader will notice some conflict and overlapping between the various contributions to this symposium. The contrast between the precision of laboratory and epidemiological methods of investigation and the intuitive methods of the clinician are manifest. Anyone concerned with the subject of chronic bronchitis will find stimulus and interest in these articles.

C. M. Fletcher

CHRONIC RHEUMATISM

KELLGREN, J. H. **Osteoarthrosis in Patients and Populations.** *Brit. Med. J.* 1961, July 1, 1–6, 8 figs. [19 refs.]

This paper is " Based on a Honyman Gillespie Lecture delivered in Edinburgh on November 3, 1960. The terms of the lecture preclude the mentioning of experiments on animals ".

Osteoarthrosis which " can be defined as an expression of a joint's inadequacy to meet the mechanical stress placed upon it " is in certain patients and in certain joints dominantly caused by abnormal mechanical factors. " But are such joints representative of the total problem of degenerative joint disease? May there not be important constitutional factors which predispose to premature degeneration of multiple joints submitted to no more than average mechanical stress?"

There follows a review of some of the information obtained in recent years from the study of population groups by field-surveys, which have been carried out particularly at the town of Leigh in Lancashire on miners and men in other occupations and on women from mining and non-mining families. The information obtained is clearly reviewed in considerable detail and discussed with a number of illustrative figures. Osteoarthrosis in patients as distinct from populations is also considered in terms of the type of the disease and the particular joint or joints affected.

In the conclusions to this paper it is stated " osteoarthrosis in women is predominantly a polyarticular condition resulting from inherited constitutional factors which may also be influenced by diet and other environmental conditions. In men the same causative factors may operate; but trauma, occupational stress, and mechanical factors in the joints probably play a predominant part ". The opinion expressed is that further epidemiological and experimental researches are urgently needed but that the future prospects for prevention and medical treatment may be good. *M. E. Delafield*

SMYTH, C. J., BLACK, R. L., DEMARTINI, F. E., DUFF, I. F., ENGLEMAN, E. P., GRAHAM, D. C., MONTGOMERY, M. M., POLLEY, H. F., ROSENBERG, E. F., SACASA, C. F., STEINBROCKER, O., WAINE, H. & WILSON, G. M., Jr. **Rheumatism and Arthritis: Review of American and English Literature of Recent Years (Thirteenth Rheumatism Review).** *Ann. Intern. Med.* 1960, Dec. 30, v. 53, No. 7, 1–365. [3455 refs.]

CANCER

MACKENZIE, A., BROWN, W. M. C., DOLL, R. & SISSONS, H. A. **Mortality from Primary Tumours of Bone in England and Wales.** *Brit. Med. J.* 1961, June 24, 1782–90, 3 figs. [18 refs.]

This study is based on records of all deaths attributed to malignant bone tumours which ocurred in England and Wales in the 3 years 1951–53 among persons aged 65 years and under. For each death certificate further details as to nature of diagnosis were sought from the doctor who signed the certificate or from the hospital in which the patient died. These additional details were obtained for 990 cases (84·7% of a total 1,169). It was considered that 516 (52·1%) had been correctly, and 449 (45·4%) wrongly, certified as dying from a primary bone tumour. In the remaining 25 (2·5%) the diagnosis was uncertain. Further analysis demonstrated that among the factors influencing the accuracy of diagnosis were place of death (hospital or elsewhere), sex, age, site of tumour, presence of Paget's disease, or in its absence, the histological type specified. The most important factor in determining the reliability of the diagnosis was the certifying doctor's pathological description of the disease.

The data from the 990 cases in which further information was obtained about the cause of death were used to estimate the number of true primary bone tumours among the remaining 179 certified cases for which no further information was available. This provided 81 additional cases of primary bone tumour and an estimated total of 597 deaths from this cause among persons aged under 65 years in England and Wales during the 3 years 1951–53. Conversion to annual mortality rates gave figures of 6·3 per 1,000,000 men and 3·9 per 1,000,000 women. These were considered minimum estimates since some of the 25 cases in which the diagnosis was uncertain were probably due to bone tumour and there may also have been some, though probably few, cases classified under other causes of death.

The peak mortality from tumours of the limb bones occured at 15–19 years of age in both sexes and at this age the male death rate was twice the female rate. Thereafter the difference between the sexes declined and rates fell with age to 34 years before rising again. The increase at ages over 40 years was largely due to tumours associated with Paget's disease. For tumours other than limb bones the age specific rates showed only a slight peak at ages 20–24 years and no difference between the sexes until age 45 years when, though female rates remained fairly constant, male rates showed a sharp increase with age.

J. T. Boyd

HUEPER, W. C. **Carcinogens in the Human Environment.** *Arch. Pathology.* 1961, Mar. & Apr., v. 71, Nos. 3 & 4, 237–67; 355–80. [Numerous refs.]

The growing pollution of the environment with chemical and physical agents associated with modern industrial development may be a serious problem of public health. Many of the substances are known to be carcinogenic to animals and the following are known to be carcinogenic to man: arsenic, asbestos, chromium, nickel, aromatic amines, benzol, isopropyl oil, mustard gas, anthracene, coal tar and pitch, creosote, industrial, commercial and domestic soots, mineral oils (petroleum, shale and lignite oils, greases and solvents), petroleum asphalt and bitumen; lignite, shale oil, synthetic hydrogenated coal and Bergius oil tars; paraffin and petroleum waxes; ionizing radiations and ultraviolet radiation. The author gives a table extending over 11 pages showing the industrial operations which use these substances and the population groups which may be exposed to them. Other experimental carcinogens should be regarded as "potential human carcinogens", until shown not to be and their presence in articles of general consumption is undesirable.

The author defines a carcinogen and considers several methods of classification—*i.e.* according to chemical nature, the organ affected, potency or completeness. He regards a carcinogen as producing an irreversible effect on cells which may, however, have to be exposed to additional factors before a cancerous growth becomes evident. In his view it is impossible, with existing methods, to determine the upper limits of a safe dose, so that the only safe dose must be regarded as zero.

Potential sources of environmental exposure to carcinogens include foods, household goods (paints, detergents, etc.), domestic and general air polutants, materials used at work, personal habits, medicines and natural infections. The sources of exposure in foods are considered in detail. Some possibly dangerous substances are added to food intentionally—*e.g.* auramine, butter yellow, etc., for colouring. Others are added as emulsifying agents, sweeteners, flavouring agents, anti-foaming agents, humectants or preservatives. Some petroleum derivatives (*e.g.* paraffin) are used for glazes, as fat substitutes or for coating. Other substances are added unintentionally, having been used on the growing plant or animal as a pesticide, or growth regulator. They may be included through the contamination of water supplies, in wrapping or as a result of incomplete combustion; the author has, for example, found measurable quantities of 3,4-benzpyrene in roasted coffee.

Richard Doll

PAPANICOLAOU, G. N., BRIDGES, Emma L. & RAILEY, C. **Degeneration of the Ciliated Cells of the Bronchial Epithelium (Ciliocytophthoria) in its relation to Pulmonary Disease.** *Amer. Rev. Respiratory Dis.* 1961, May, v. 83, No. 5, 641–59, 14 text figs. & 28 coloured figs. on pl. [17 refs.]

Microscopic examination of sputum specimens shows that in some patients there is extensive degeneration of the ciliated cells of the bronchial epithelium. This degeneration may conveniently be described as "ciliocytophthoria" (CCP). CCP is indicated by 3 principal abnormalities: (1) the presence of fragmentary "tufts" of cytoplasm, separated from the cell nucleus, (2) pyknotic nuclei, and (3) nuclei showing chromatin lumping; all these abnormalities may be accompanied by acidophilic inclusion bodies in the cytoplasm.

The significance of CCP has been investigated by

examining sputum specimens from 500 patients routinely attending a cancer detection clinic and principally asymptomatic (A series) and 500 patients attending hospital or a private physician with symptoms suggesting the possibility of bronchial cancer (B series). Normal subjects were defined as persons in the A series with normal clinical findings and chest X-ray and without evidence of abnormal cells in a sputum examination for malignancy and excluding those who developed an acute upper respiratory infection within 3 months. The results were expressed as the proportion of persons in each clinical category whose sputum specimen showed more than the "normal" average number of (i) "tufts", (ii) pyknotic nuclei, and (iii) nuclei with chromatin clumping.

Both series showed a greater proportion of CCP among persons with acute and chronic respiratory conditions, but the acute patients in series A showed a higher proportion with abnormal counts (49% tufts, 54% pyknosis and 54% clumping) than those in series B. This is attributed to the prevalence of an epidemic of Asian influenza at the time of examination of the A series. An excess incidence of abnormalities was shown by slightly more of the patients with malignant disease in the B series than by the corresponding patients with inflammatory disease. It is suggested that the mass destruction of ciliated cells in pulmonary infections may predispose to the action of extraneous carcinogens. *Richard Doll*

SIEVERS, M. L. & COHEN, S. L. **Lung Cancer among Indians of the South-Western United States.** *Ann. Intern. Med.* 1961, May, v. 54, No. 5, 912–15.

In 12,511 hospital admissions of south-west American Indians during the years 1954–60 there were 87 cases of malignancy, none of which involved the lung. More than 50,000 chest X-ray films of the same population were examined in the same years and no primary pulmonary malignancy was detected. Either hereditary or environmental factors may contribute to this situation. There is apparently very little contamination of the air by industrial fumes in the reservations and cigarette smoking is much less frequent than among Caucasians.

Austin Bradford Hill

WILLIS, R. A. **The Incidence and Histological Types of Pulmonary Carcinoma, with Comments on Some Fallacies and Uncertainties.** *Med. J. Australia.* 1961, Mar. 25, v. 1, No. 12, 433–40. [Numerous refs.]

The author discusses the validity of two beliefs: (1) that there has been a real increase in the incidence of carcinoma of the lung, and (2) that the condition can be divided into several histological types, which differ in their aetiology and behaviour.

Between 1900 and 1952 the mortality attributed to lung cancer in Britain increased 40 times and the question has to be considered whether this increase can be due to improved diagnosis. Certainly many cases were misdiagnosed in the past. During 1881–1900 the Transactions of the Pathological Society of London, for example, contain records of 34 cases which were almost certainly cases of bronchial carcinoma. Yet the diagnoses were mediastinal tumour 12, lung carcinoma 8, other tumours of lung, 4, pleural tumour 2, abdominal tumour 6, brain tumour 1, disseminated cancer 1. Since there were so few correct diagnoses after autopsy, it must be presumed that the proportion of correct diagnoses in general will have been very much lower. During the next 30 years pathologists realized that lung cancer was not a rare disease and in 1926 Barnard showed that what had been described as "oat-cell sarcomas" were, in reality, carcinomas. Studies of autopsy data showed that during this period there was little or no evidence of an increase in the proportion of cases in which intrathoracic cancers were discovered. During 1931–60 autopsy data showed an increase of about 50%; but the recorded mortality increased 10-fold. This difference is so striking that neither result should be relied on. Recent autopsy studies continue to show that many cases are missed (as many as 29% in one study in 1956) and the author has no difficulty in believing that at the beginning of the century 95% may have been wrongly certified.

Examination of the published data on the different histological types of bronchial carcinoma shows a wide divergence between the results obtained by different investigators. For example, the proportion of adenocarcinoma in men varies from 3 to 31% and in women from 13 to 67%; similarly the proportion of squamous carcinomas varies from 19 to 60% in men and from 7 to 15% in women. This is not surprising because many tumours provide evidence of more than one histological type and there is often variation between the appearance of sections from different parts of the same tumour and between the appearance of the primary and of secondaries. There are theoretical objections to the separation of squamous cell and adenocarcinomas of the bronchi, since both arise from normally non-squamous epithelium and squamous characteristics must be presumed to have arisen from metaplasia, which might equally well arise in the tumour as in the pre-malignant epithelium.

The author does not deny that there may have been some real increase in lung cancer, or that it may have been predominantly in males, or in one histological type; but it is unwise to assume that these changes have occurred. *Richard Doll*

MISCELLANEOUS DISEASES

PUCHLEV, A., POPOV, N., ASTRUG, A., DOTSCHEV, D. & PETRINSKÀ, S. Über die endemische Nephritis in Bulgarien. **[Endemic Nephritis in Bulgaria]** *Schweiz. med. Woch.* 1961, June 24, v. 91, No. 25, 751–6, 6 figs. [25 refs.]

An endemic renal disease which is generally called "Endemic Nephritis" occurs in 2 neighbouring areas of Bulgaria the geography of which is described. The disease exists in about 20 villages in these areas and it is noteworthy that it is restricted to these villages and does not involve the many other villages which are in the immediate neighbourhood.

This paper contains a full account of investigations in 14 of the affected villages where in 1954–58 among an aggregate population of about 19,000 there were 1,116 deaths of which 258 (23·1%) were due to renal disease. Clinical examination was made of 74 patients. The proportion of females was 59·5% as against 40·5% of males. Only persons over 20 years of age are affected and the highest incidence is in the 30–60 year age-group.

Onset of the disease is slow with dull pain in the lumbar region but sometimes symptoms similar to those of renal colic. The condition of the patient gradually deteriorates and in spite of treatment death always occurs.

There is a description of the laboratory and clinical examinations which were carried out. Many tests of renal function were made. Blood examinations were also included as marked anaemia occurs early in the disease. Full accounts with photographs of the post-mortem appearances of the kidneys are given.

In general the picture of the disease is that of a chronic nephropathy without oedema, hypertension or retinal changes but with marked anaemia. In the urine there is very slight albuminuria but the renal clearance tests indicate early involvement of the tubules and later of the glomeruli. At post-mortem the kidneys were seen to be small and smooth with degenerative changes in the tubules and glomeruli. Polypoid changes, papillomata and carcinoma of the urinary tract were associated conditions in nearly half the cases.

Investigations were done in the attempt to discover the aetiology of the disease but all with negative results. These included bacteriological, virological and mycological examinations, chemical tests of water and soil for toxic constituents and even the cattle of the district were examined for the presence of renal disease.

It is suggested as a possibility, however, that the cause of the disease may be the association of 2 heavy metals such as uranium and lead in the water each present in a minute non-toxic concentration which may nevertheless potentiate the toxicity of the combination.

M. E. Delafield

Sanitation

The order in this section is:—**General; Water and Swimming Baths; Sewage, Trade Waste and Refuse Disposal; Housing; Infestation; Atmospheric Pollution; Port, Ship and Aviation Hygiene.**

WATER AND SWIMMING BATHS

(Including the Bacteriology of Water Supplies)

DOBBERKAU, H. J. Zur hygienischen überwachung und Beurteilung mineralwasserverarbeitender und limonadenherstellender Betriebe. **[Hygienic Supervision and Appraisal of Mineral Water and Lemonade Bottling Plants]** *Ztschr. f.d.g. Hyg. u. ihre Grenzgebiete.* Berlin. 1961, Apr., v. 7, No. 4, 241–8, 3 figs.

The author points out that even today mineral water manufacturing plants can still be sources of danger and the situation can be improved by an increased understanding on the part of employees of the hygienic problems connected with their work. From his personal experience and investigations and from instances cited in the literature the author draws attention to some of the hazards involved.

Experiments were carried out in a mineral water plant by using bottles into which a suspension of *Escherichia coli* had been introduced deliberately. It was found that in lemonade containing lactic acid, with a *p*H of 3·2, considerable concentrations of *E. coli* were destroyed in 20 hours. Experiments showed that the other components of the lemonade were not responsible for this effect.

E. Windle Taylor

D'ARCA SIMONETTI, A. Indagine batteriologica sulle acque minerali imbottigliate. **[A Bacteriological Investigation of Bottled Mineral Waters]** *Nuovi Ann. d'Igiene e Microbiol.* 1960, Nov.–Dec., v. 11, No. 6, 497–506. [26 refs.] English summary (6 lines).

The author mainly concerned himself with examining bottled waters as they are normally available for sale, though this would not necessarily indicate the nature of the water at bottling. 73 samples on sale in Rome produced by 9 firms were examined between November 1958

and October 1959. After adjusting the *p*H of the sample to 7, when necessary, counts were made in gelatin at 20°C. and in agar at 37°C. Coliform bacteria were sought in 300 ml. samples by seeding 2 volumes of 100 ml. and 10 of 10 ml. in lactose peptone water, subculturing on Levine's medium, and identifying further. Counts were made on McCrady's most probable number technique. For anaerobic spore-bearers a liver broth culture method was used.

Tests for free chlorine were negative. 27% of the samples examined showed at least one of the characters on which a water supply would be judged adversely, most commonly showing too high a total count at 37°C., and least often through the presence of coliforms. These were most often intermediate I and II and *Bact. aerogenes* I and II. Only once was *E. coli* found at 20 per ml. The author believes that the bottling procedures are most often to blame for contamination of an originally pure water.

E. Agius

D'Arca, A., Sebastiani, L. & Lionetti, V. Indagine batteriologica sull'acqua dei serbatoi domestici nella città di Roma. [**A Bacteriological Investigation of the Water in House Tanks in Rome**] *Nuovi Ann. d'Igiene e Microbiol.* 1960, Nov.–Dec., v. 11, No. 6, 507–18. English summary (6 lines).

This investigation was undertaken because a notable proportion of the inhabitants use, for drinking, water which has been in tank reservoirs in the house. The only chemical examination carried out was that for the determination of free chlorine, water in Rome being normally chlorinated. 237 samples were examined of which 206 were from house tanks and 31 from street mains, some of which were those which supplied the tank water from which unfavourable results had been obtained. Samples were mainly taken from houses built before 1940, scattered throughout the different quarters. Tanks were mainly situated on the roofs. Counts were made on gelatin at 20°C. and on agar at 37°C. Coliforms were counted, as also were anaerobic spore-bearers. Most of the results obtained, which varied widely and included a number of bad ones, are given in a lengthy table. No typical *Escherichia coli* was found. Free chlorine was almost always present but in very small concentrations.

E. Agius

D'Arca Simonetti, A. & Aurizi, A. Le acque di soda in vendita nella città di Roma (Indagine batteriologica.) [**Bacteriological Investigation of Soda Water on Sale in Rome**] *Nuovi Ann. d'Igiene e Microbiol.* 1960, Nov.–Dec., v. 11, No. 6, 533–40. [21 refs.] English summary (4 lines).

Soda water—drinking water with added sodium bicarbonate and supersaturated with CO_2—is used in siphons which, though easily refilled, are cleaned with difficulty and always retain some of their previous contents which become laden with bacteria. 3 previous papers on the subject are quoted which consider the purity of soda water and come to adverse conclusions.

80 soda water siphons, taken from 58 bars between October 1958 and May 1960 were sampled by using the same technique as adopted by D'Arca Simonetti for mineral waters [see p. 969]. Results for agar and gelatin counts, coliforms and anaerobic spore-bearers are given in 4 tables; 63 samples gave results at least one of which, with mainly high agar and gelatin counts, would have caused a water supply to be considered adversely. Typical *Escherichia coli* was found in 2 samples.

The authors conclude that no progress appears to have been made in the preparation of soda water in siphons since 1895 in spite of various regulations, including some contained in a presidential decree as recent as 1958. Observance of such rules would suffice to improve matters.

E. Agius

Saalbreiter, R. & Lingelbach, H. Silowasser als Ursache von Brunnensperrungen. [**Silo Effluent as a Source of Pollution of Wells**] *Ztschr. f.d.g. Hyg. u. ihre Grenzgebiete.* Berlin. 1961, Apr., v. 7, No. 4, 248–57, 3 figs.

Drainage from silos, the authors state, has until recently been little considered as a source of pollution of drinking water. The effluent from maize silos has a high organic content and contains appreciable amounts of iron and manganese. In the autumn of 1960 several wells in the area of the Hygiene Institute of Karl-Marx-Stadt were contaminated by silo drainage and became unsuitable for public supply. In some cases the contamination lasted for several months. The taste and bacteriological threshold for contamination by maize silo effluent is stated to represent a dilution of 1 in 10,000.

The authors recommend the collection of silo effluent in pits, before use as a fertiliser, as a measure likely to reduce the danger of contamination of gathering grounds, and that the sanitary authority should be consulted in the selection of suitable sites for silos.

E. Windle Taylor

Kelly, Sally & Sanderson, W. W. **Enteric Viruses in Wading Pools.** *Pub. Health Rep.* Wash. 1961, Mar., v. 76, No. 3, 199–200.

During July and August 1959 4 wading pools in Albany, New York, were examined for enteroviruses by techniques devised by the senior author [this *Bulletin*, 1954, v. 29, 890]. Viral agents (2 ECHO 11 and 4 ECHO 3) were isolated from 6 samples—3 from 1 pool, 2 from the 2nd pool, 1 from the 3rd pool and none from the last pool. This negative pool was the one with the lowest coliform count. It is noted that these pools were not chlorinated like swimming pools from which no viruses were isolated. Such chlorination is advocated also for wading pools.

A. J. Beale

SEWAGE, TRADE WASTE AND REFUSE DISPOSAL

MINISTRY OF HOUSING & LOCAL GOVERNMENT. **Pollution of Water by Tipped Refuse. Report of the Technical Committee on the Experimental Disposal of House Refuse in Wet and Dry Pits.** 141 pp., illustrated. [24 refs.] 1961. London: H.M. Stationery Office. [7s.]

This is the Report of a Technical Committee appointed in 1953 by the Ministry of Housing and Local Government with the following terms of reference: "To define and generally guide experiments to be carried out at the Bushey Urban District Council's old sewage works on the tipping of household refuse of various categories under dry and wet conditions of deposit, with special reference to the pollution of underground water."

The Report is in 3 sections (a) a summary, (b) the Committee's report on and discussion of the experiments over which they had exercised a general oversight, and (c) a detailed report of the investigation by the Department of Scientific and Industrial Research, the Laboratory of the Government Chemist.

These experiments on wet and dry tipping which were of laboratory or pilot plant scale are very fully described. For example in an experiment at Bushey 90 tons of refuse were tipped into a tank and records of rainfall and percolation over $2\frac{1}{2}$ years are given with details of the chemical and bacterial composition of the percolates and a computation of the amount of polluting matter leached from the refuse in this period.

In the Committee's summary it is stated "The matter has proved exceedingly complex and it is quite impossible to prepare a short technical summary of our conclusions which would be useful and not at the same time liable to be misleading. It is essential that anyone wishing to use our results should read the whole report." Also "it seems important to emphasise here that, overall, our work constitutes no condemnation of controlled tipping. It is generally a satisfactory method of refuse disposal and there is no reason why it should not continue to be widely used". It may also "now be possible, with appropriate safeguards, to bring into use sites hitherto considered unsuitable". *M. E. Delafield*

SIGNORINI, L. F. Il problema sanitario dello smaltimento dei rifiuti liquidi industriali. [**The Sanitary Problems of the Disposal of Liquid Industrial Wastes**] Presented at XXI Congresso Nazionale d'Igiene, Firenze, 21–24 ottobre 1959. 116 pp., 3 figs. [166 refs.] 1960. Rome: Associazone Italiana per l'Igiene e la Sanità Pubblica.

The author is on the staff of the Institute of Hygiene in the University of Florence: he presented this report to the 21st National Health Congress which was held in that city in October 1959. He starts by referring to the close connexion of his subject with the problem of satisfying the ever-increasing demands for water supplies, more especially when these are, as often, derived from surface waters. In the last 100 years the world population has increased from 1,170 million to over 2,700 million and its present rate of increase is 45 million a year. The rising standard of living of an ever-increasing proportion of an even larger world population involves a growing demand for domestic and industrial water supplies and for the products of industry, and the output of liquid industrial wastes into surface waters goes on increasing in quantity and variety.

Signorini discusses the general characteristics of these liquid industrial waste products which may, *inter alia*, carry pathogenic micro-organisms, putrescible and poisonous substances and other harmful matter. In a table he sets a series of inorganic and organic substances against the types of industrial plant which discharge them into surface waters as waste: another table deals with the waste output of some of these plants in quantitative terms. He discusses the chemical processes and changes which these waste substances undergo in the surface water and their effect on its biological and on its organoleptic characteristics: hence the harmful effects which may arise from the use of surface waters which have been so polluted and the resulting public health problems.

In another table the author lists 11 radioactive elements and indicates the type of radiation which each emits and the half-life in each case. He refers to the risk from waste effluents which contain inflammable or explosive material and deals with the problems which have been created by the wide use of detergents. He classifies the forms of life which are to be found in surface waters, including "sewage fungus" but excluding the vertebrates, and he touches on the effects of industrial waste pollution in relation to fish supply.

The author quotes tolerance limits (in parts per million of drinking water) which the U.S. Public Health Service has laid down for various metals and bases and he refers to other quality standards and other practices in the classification of surface water supplies in certain countries outside his own. He then examines the problem as it arises in Italy. He reproduces a long questionnaire which his Institute has recently sent out to 578 public health authorities in Tuscany: only 164 of these forms were returned, 69 being incompletely filled, and only 57 indicated that there was any known public health problem.

The paper concludes with a brief discussion of certain control measures which, in the author's view, should help to cope with the problem as it exists in Italy.

J. Cauchi

MAJUMDER, N. & SENGUPTA, J. N. **A Latrine for Use in Rural Areas.** *Indian J. Pub. Health.* 1960, Oct., v. 4, No. 4, 201–6, 3 figs.

The Indian Council of Medical Research financed an investigation of the various types of rural latrine locally in use with a view to evolving a satisfactory and cheap type. Common defects found in the latrines tested were failure to flush effectively with small quantities of water, splashing of water in the trap and of urine on the slab. Modifications of existing types led to a more suitable design. It is a pour-flush latrine discharging into a pit

3 ft. wide by 10 ft. deep. The pan is designed to receive the faeces directly into water and so prevent fouling and reduce the amount of flushing water. Details of the measurement of pan and trap are shown in diagrams. The water trap seal is only 5/16 of an inch and hence careful construction of the neck and trap is needed. The pan can be cast in one piece, and the trap in 2 subsequently grouted with cement. Quantities of materials required are given for cement-finished and mosaic-finished pans, the latter giving a smoother surface. The cost of the latrine is about Rs.15 which is prohibitive for villagers. It is recommended that the installation of latrines of this type should be subsidized and that the price be reduced by mass production. *T. H. Davey*

HOUSING

WEBB, C. G. **The Diurnal Variation of Warmth and Discomfort in some Buildings in Singapore.** *Ann. Occup. Hyg.* London. 1961, June, v. 3, No. 4, 205–18, 17 figs. (2 on 2 pls.)

Malayan houses are unheated, and cooking is commonly done outside. The houses are well shaded from the sun, and are often so orientated as to minimize the solar heat load. They are well ventilated, with large unglazed windows and other openings, and often have open-work material for some of their walls. The floors may be only loosely boarded, and the roofs lightly thatched. In such buildings ventilation rates are high, and possibly 10 times as high as is common in England. The thermal capacity of the buildings is low.

Observations were made of the diurnal variations of the thermal environments in 14 buildings in Singapore in the period 1949–50, and the results obtained are shown in graphic form.

Wet-bulb temperatures ranged from 75 to 86°F. At 6 a.m. the average value was 76°F., and at 9 a.m. the typical daytime average of about 80°F. was reached.

Dry-bulb temperatures of 78 to 92°F. were observed. The average peak temperature reached in the afternoon was 86 or 87°F., and the night minimum was about 79°F. In buildings with non-metallic roofs the temperature shown by the globe thermometer rarely differed from the dry-bulb temperature by more than 1°F., so that in such buildings radiation effects were slight.

The relative humidity was always high. It was lowest in the afternoon when it averaged 80%, and during the night it averaged 89%.

Air speeds indoors were low. The maximum, at 5 p.m., averaged about 50 ft. per minute, and through the night the average was only 16 ft. per minute.

Discomfort due to excessive warmth was common at all times except from 2 to 8 a.m. Apart from a brief period at about 4 to 5 p.m., discomfort from cold only occurred between midnight and 7 a.m. At almost any time the total incidence of discomfort was nearly 50%.

Finally the author refers to his Equatorial Comfort Index, and reproduces the nomogram for its estimation.

Thomas Bedford

CENTRAL OFFICE OF INFORMATION. Reference Pamphlet No. 39. **Housing and Town and Country Planning in the U.K. Dependencies.** 54 pp., 20 figs. on 8 pls. 1960. London: H.M. Stationery Office. [3s. 6d.]

ATMOSPHERIC POLLUTION

GOLDWATER, L. J., MANOHARAN, A. & JACOBS, M. B. **Suspended Particulate Matter. Dust in "Domestic" Atmospheres.** *Arch. Environment. Health.* Chicago. 1961, May, v. 2, No. 5, 511–15.

30 samples of the particulate matter in domestic atmospheres in the New York area were taken at flow rates around 55 cu. ft. per minute; the locations included offices, living-rooms, bedrooms and laboratories and information is given about floor-covering, furnishing and frequency and method of cleaning. The samples were taken during February and March with windows closed before and during operation. The outdoor air was sampled immediately after the indoor atmosphere.

Results are expressed as total suspended particulate matter in μgm. per m.^{3} and as percentage ash content. There is no correlation with indoor conditions.

On the average the concentration indoors was a little over two-thirds of that outside while the indoor ash content was less than half of the outdoor. Indoor air was thus cleaner than outdoor in terms of total suspended solids and liquids but the proportion of organic material was higher indoors.

The analysis is taken no further than this but it is probable that the differences are largely due to there being more siliceous matter in the open air and more animal and vegetable fibres in dwellings [DAVIES, *Dust is Dangerous*, this *Bulletin*, 1955, v. 30, 377].

C. N. Davies

SALEM, H. & CULLUMBINE, H. **Kerosene Smoke and Atmospheric Pollutants.** *Arch. Environment. Health.* Chicago. 1961, June, v. 2, No. 6, 641–7, 3 figs. [18 refs.]

The purpose of this work was to find out whether kerosene smoke altered the effects of inhaling sulphuric acid aerosols (mass median diameters 1·2 and 0·5 μ), sulphur dioxide, acetaldehyde and acrolein.

In the experiments described 620 mice, 100 rats, 430 guineapigs and 30 rabbits were exposed, some to the individual contaminant, some to kerosene smoke for 6 hours and then to the individual contaminant 3 days later, and some to both together. The behaviour and time to death for each animal were recorded and autopsies carried out. Exposures are expressed by the product of concentration and time, in the units milligramme-minutes per cubic metre (mgm.-min./cu. m.).

Massive concentrations were used, up to 174 mgm./cu.m. of sulphuric acid and over 2,000 mgm./cu.m. of the other pollutants: kerosene smoke did not prove toxic, but for the other contaminants the longest mean time to death which is recorded is less than 9 hours and the shortest only 11 minutes.

The authors conclude that kerosene does not modify the toxicity of contaminants if it is given beforehand, but that given simultaneously it may increase or decrease it, or leave it unchanged. They appear to base this conclusion on a probability P appearing in their tables but nowhere described and only once mentioned in the text: presumably this P is derived from a comparison of the mean fatal doses with and without the kerosene smoke, by using STUDENT'S t-test.

The reviewer doubts the relevance of experiments involving such enormous concentrations to any real situation, but the authors state that long-term exposures are now in progress, in which contaminant concentrations up to 1 p.p.m. only are used. *J. McK. Ellison*

Occupational Hygiene

The order in this section is:—**General; Occupational Physiology; Occupational Diseases (Dust Diseases, Poisoning, Skin Diseases, Others); Occupational Psychology; Heating, Lighting and Ventilation.**

GENERAL

MEIKLEJOHN, A. **Occupational Health in Egypt: a Traveller's Impression.** *Trans. Ass. Indust. Med. Officers.* 1961, Apr., v. 11, No. 1, 16–21, 2 figs.

This is a candid and vivid description of the condition of industrial and other affairs in Egypt at the present time, and of the efforts being made to improve the lot of the worker. Egypt is a poor, disease-ridden country, with a population increasing and accumulating in the over-crowded parts of the land. A not very flourishing agriculture is the main industry, but new factories for oil refining, production of fertilizers, motor assembly and so on are being started and these, with a revival of the tourist trade, provide the hope for the future.

The object of the government is to provide an occupational health service and later to develop a health service. Hours of work are regulated by law and wages are controlled by committees composed of representatives of the government, of employers and of the workmen. All factory employers must provide first aid facilities. Factories employing 100–500 workers must employ a physician and a male nurse: hospital treatment must be paid for by the employer. Certain industrial accidents and 24 prescribed diseases are notifiable. There is a shortage of doctors. The output of doctors is to be raised to 1,000 per annum at 3 medical schools. A High Institute of Public Health has been established at Alexandria to give public health training to doctors and engineers, and training is given in occupational hygiene in the second part of the course. Dr. Meiklejohn's review is a comprehensive one: moreover he imbues the reader with his sympathetic attitude to Egypt's difficulties. *Charles L. Sutherland*

COMMITTEE ON INDUST. MED. RECORDS & COUNCIL ON OCCUP. HEALTH. **Guide to the Development of an Industrial Medical Records System. Part I.** *Arch. Environment. Health.* Chicago. 1961, June, v. 2, No. 6, 705–13, 3 figs. (2 folding).

JONES, J. G. **An Investigation into the Effects of Exposure to an Oil Mist on Workers in a Mill for the Cold Reduction of Steel Strip.** *Ann. Occup. Hyg.* London. 1961, June, v. 3, No. 4, 264–71.

During the cold reduction in a 3-stand tandem rolling mill of coils of hot rolled strip steel it was noticed that a certain amount of oil was carried into the atmosphere from the evaporation of some of the water coolant used in the process of rolling. Possible ill effects from the inhalation of an oil-contaminated atmosphere are:—Pulmonary—lipoid pneumonia, increased liability to develop focal pneumonia, bronchitis, long-term fibrotic changes, and carcinoma; gastric—hyperplastic gastritis; ear, nose and throat conditions—rhinitis, sinusitis, pharyngitis and laryngitis; skin affections—dermatitis

and oil acne. It was accordingly decided to investigate the matter. The process is briefly described and the air temperature readings obtained at different stages in the process and at different points are listed: the range was from 75°F. up to 215°F. The oil consisted of about 85% of a napthenic spindle oil with petroleum sulphonates and rosin soaps acting as emulsifiers and with a small proportion of cresylic acid as a disinfectant. Oil distillation tests showed that a temperature of 160°F. was necessary before any volatile compounds were observed, and only at 200°F. was 0·80% distillate obtained but at 200–210°F. a white vapour was given off which had a pungent and unpleasant smell and solidified in the condenser. Estimation of oil in the atmosphere showed the maximum concentration to be 9·0 μgm. per litre and 70% of the droplets measured 0·8 to 1 μ in diameter. The total number of men exposed to risk was 84 and of these 19 volunteers were interviewed about their occupational histories, medical histories and present syptoms. A general physical examination including X-ray of chest was carried out.

The results of these investigations are reviewed and no evidence of obvious disease was found although in 12 cases increased linear striations were noted in the radiographs. No reports of similar investigations could be found in the literature but two papers are quoted indicating the results of experiments carried out on animals, and the findings are discussed. In the present investigation the oil is carried in the atmosphere unchanged but droplet sizes are such that penetration into the lungs and retention in the alveoli probably occur so that the possibility of long-term fibrotic changes is theoretically obvious and requires consideration in the light of the X-ray findings in this study. Although no evidence of occupational disease was found there may be other industrial processes in which the concentration of oil is higher, the exposure longer, and where harmful effects may occur. *G. F. Keatinge*

Bühlmann, A. A. La physiologie respiratoire au cours de la plongée sous-marine. **[Respiratory Physiology in Diving]** *Schweiz. med. Woch.* 1961, July 1, v. 91, No. 26, 774–8, 5 figs.

The respiratory problems of diving are considered in the light of recent researches on the phenomena of laminar and turbulent air-flow, on the resistance to flow in the respiratory tract, and on the work of the respiratory muscles.

In the respiratory tract the flow of air is partly laminar and partly turbulent, and as the pulmonary ventilation rate rises the turbulent fraction increases greatly. Thus, with increase in ventilation the viscous resistance is notably increased, and the resultant increase in respiratory work bears a logarithmic, and not an arithmetic, relation to the ventilation rate. In swimming, for instance, one may breathe at the rate of 60 litres per minute as compared with 10 at rest, but the respiratory work will not be 6 times as great as that at rest, but 36 times.

If the respiratory work required is too great the ventilation rate will be reduced, with consequent hypoventilation and retention of carbon dioxide. The author interprets the symptoms of the so-called nitrogen narcosis as the consequences of hypercapnia and respiratory acidosis. The high oxygen tension, when diving is done with compressed air, promotes the tendency to hypoventilation.

To avoid nitrogen narcosis during deep dives there is a choice of 2 methods: the replacement of nitrogen by a light inert gas such as helium; or the use of artificial respiration to reduce the energy expenditure of the respiratory muscles. The author concludes that there is no specific narcotic effect of nitrogen at high pressures.

Thomas Bedford

Rózsahegyi, I. & Gömöri, B. Otologische Untersuchungen bei Caissonarbeitern. **[Aural Examination of Caisson Workers]** *Arch. f. Gewerbepath. u. Gewerbehyg.* 1961, v. 18, No. 4, 384–93. [21 refs.]

The investigations here described were undertaken to provide information on the question of whether the inner ear which is particularly sensitive to the strain of decompression in caisson work may suffer damage without there being any subjective symptoms in the workers concerned.

There is a full account of the methods adopted and the results thereby obtained in the aural examination of 131 workers who had suffered from decompression sickness and 52 men also engaged in caisson work who at periodic control examinations had no symptoms or signs of illness referable to their work.

The findings, which are described with tables of results and also fully analysed and discussed, demonstrate that in both groups of caisson workers there was damage both to the cochlear and vestibular functions but that this damage was significantly greater in those men who had suffered from decompression sickness.

M. E. Delafield

Nashimoto, I. & Furuhashi, M. Un cas de pneumothorax spontané chez un travailleur en caisson. **[Spontaneous Pneumothorax in a Caisson Worker]** *Maroc Méd.* 1961, May, v. 40, No. 432, 522–5, 7 figs.

Krynsky, O. M. & Musikhin, L. S. **[Coronary Insufficiency as a Sequela of Industrial Electrical Injuries]** *Gigiena Truda i Professional'nye Zabolevaniya.* Moscow. 1961, v. 5, No. 5, 55–7, 2 figs.

Two patients presenting evidence of coronary insufficiency following electric shock were seen soon after one another at the same hospital.

Patient B, aged 32, was admitted 1½ hours after contact of the hands with a loose electrical connexion. He lost consciousness on touching the live wire and remained unconscious for 1½–2 hours. Apart from a burn no other changes were discovered on admission. The day after the accident he complained of aching in the heart region and on the 3rd day the heart sounds, previously normal, became muffled. The body temperature

remained normal but the blood picture showed a slight monocytosis. In the 3rd week tachycardia (pulse rate 120) appeared—a radio-iodine test showed normal thyroid function, the blood cholesterol was 200 mgm. and the prothrombin 96·3%. At the end of the second month symptoms of disorder of the central nervous system appeared; irritability, weakness of ocular convergence, weakness of muscle power of the left extremities and clonus of the left foot. There was also dyspnoea on physical exertion and pain in the cardiac region on long standing. Treatment which included rest, dicoumarin and vitamins did not result in complete disappearance of these findings.

Electrocardiographic [ECG] findings were as follows: On the day of admission, only a high, symmetrical T wave in V_2 gave rise to the suspicion of insufficiency in the region supplied by the right coronary artery. In the next few weeks T_3 and Tav became inverted and symmetrical and T v_2 was increased from 0·76 to 1·25 of the R wave, confirming ischaemia of the posterior wall of the left ventricle. In the course of 15 months the T_3 and Tauf waves assumed a more normal shape and the ECG became almost completely normal.

Patient L, aged 26, was admitted after an accident in which he touched a live surface with the right hand. Immediately after contact he lost consciousness for 10–15 minutes and there were convulsive movements involving all the skeletal muscles. "Current marks" were found on the right palm but no pathological changes of the internal organs. After 10 days the patient complained of dyspnoea on walking and praecordial pain. The blood pressure was 115/85, the heart sounds were muffled but there was no objective evidence of cardiovascular insufficiency. Blood cholesterol was 170 mgm.%, the patient was apyrexial and the blood picture normal. After treatment by rest and Pyramidon the patient's condition improved but pain and dyspnoea remained for 1–2 months. It was nearly 6 months before his condition became normal.

Examination of the serial ECG records shows that a week after the accident the T waves in V_2 and V_4 leads increased in size and became symmetrical and pointed (the height of the T wave compared with the R wave was 2:1 on admission, 6 days later it was 5:1). This indicated ischaemia of the posterior wall of the left ventricle. It is claimed that further investigation over the subsequent months showed a variable degree of coronary insufficiency apparently judged by the ECG findings.

[This is an interesting paper. Unfortunately the quality of reproduction of the ECG records makes it difficult to confirm or disprove the conclusions drawn from them.]

W. R. Lee

Ruben, H. Indblaesningsmetoden som kunstig respiration. [**Expired-Air Resuscitation**] *Nordisk Med.* 1961, July 6, v. 66, No. 27, 953–6, 4 figs. [31 refs.]

The English summary appended to the paper is as follows:—

"The most reliable non apparatus method of artificial respiration is the expired-air method. Experiences since its re-introduction 2 years ago indicate that this time it has come to stay. The practical difficulty in teaching the method for laymen has been overcome by the introduction of a training manikin. Because of its simplicity *the head-tilt method* of expired-air resuscitation has been settled for in Denmark for the use by lay rescuers. It is based on hyperextension of the head and pulling the chin up, which combined manoeuvre produces a good opening of the airpassage past the tongue. It can be used whether inflating through the mouth or the nose. In Denmark the latter is preferred as a first choice, because with it gastric inflation is smaller, thereby minimizing the risk of aspiration of stomach contents into the lungs.

"Where a rescuer is not able to (or does not want to) use an expired-air method, the manual method is the only choice. A backward tilt of the victim's head should also be aimed at with the Holger Nielsen method. If there is a bystander he should be asked to help maintain an open airpassage."

Croton, L. M. **Modern Methods of Emergency Artificial Respiration: US Firemen try New Technique.** Reprinted from *Fire Protection Rev.* 1961, v. 24, No. 247, 346–53, 3 figs. [17 refs.]

After describing artificial respiration by mouth-to-mouth breathing as developed by Dr. Peter Safar, the author refers to 44 cases of asphyxia treated by this method by New York firemen. 20 of these recovered and not one of the firemen concerned sustained any infection. Reluctance of a rescuer to apply his mouth directly to that of a victim may be diminished if a handkerchief is used to cover the victim's mouth. Evidence is quoted indicating that the use of an airway by anyone unskilled in this practice has proved dangerous.

T. O. Garland

Calvi, L. Aspetti del circolo venoso degli arti inferiori fra i vigili urbani addetti al traffico. [**Some Aspects of the Venous Circulation in the Lower Limbs of Policemen controlling Traffic**] *Med. d. Lavoro.* 1961, Feb., v. 52, No. 2, 138–43. English summary (9 lines).

The present enquiry was undertaken to investigate the prevalence of pathological conditions affecting the venous circulation in the lower extremities of policemen controlling road traffic in Milan. In addition to cases in which the veins themselves were affected, other conditions likely to cause pathological effects but not directly related to the job have been taken into account. Constitutional factors, associated pathological conditions and family and personal history have been given particular attention. 403 policemen with a continuous period of service on traffic control duties which ranged from 1 to 9 years and whose ages varied from 22 to 43 years were examined. There were 129 cases (32%) among whom anomalies of the venous circulation of the lower limbs were noted and tables are given in which the distribution of the men examined is shown in relation to age and length of service respectively.

The venous anomalies were divided into 3 categories

(i) peripheral defects without signs of stasis, (ii) cases showing early evidence of varicose decompensation with permanent dilatation of the veins and with oedema after certain kinds of exertion at work, (iii) varicosities with definite stasis accompanied for example by infiltrative cellulitis, cutaneous dystrophia or by sequelae of superficial or deep episodes of phlebitis. In category (i) there were 59 cases (14·6%) of all policemen investigated and 51 (12·6%) and 19 (4·7%) in categories (ii) and (iii) respectively. In assessing somatic characteristics the height and body weight, the relationship between height and the length of the lower limbs and that between the length of the thigh and of the leg were considered and the findings are summarized in a table. Among associated pathological diseases found in the 403 policemen examined there were 68 cases (17%) of haemorrhoids and 53 cases (13%) of varicocele. There were 104 cases (25%) of flat foot but in only 42 of these men (40%) were disturbances of the circulation noted in the lower limbs. 78 cases of lumbo-dorsal arthrosis were found, and in 36 of the subjects vascular anomalies were present in the lower limbs which are attributed in part to the frequent use of surgical belts in these conditions which, by preventing free movement of the abdomen and diaphragm, tend to bring about stasis in the lower extremities.

The implications of these findings are discussed with special reference to the criteria needed in the selection of suitable candidates for this branch of police work.

G. F. Keatinge

Schröter, G. & Schulz, G. Untersuchungen über die Dupuytrensche Kontraktur bei Bierfahrern. **[Investigations of Dupuytren's Contracture in Beer Wagon Drivers]** *Arch. f. Gewerbepath. u. Gewerbehyg.* 1961, v. 18, No. 4, 458–66, 1 fig. [44 refs.]

This paper with its numerous references contains much information on Dupuytren's contracture—its nature; frequency in different countries; incidence in various employments and at different ages; and the theories of causation which have been advanced.

The high incidence of 6 cases of the contracture (15·6%) among 38 drivers of a brewery led to the investigation of 284 men engaged at breweries in Berlin. Grouping of these men by age and length of employment showed that in a group of 102 men of average age 28·1 years and 4·47 average years of employment the number of cases of contracture was only 2 (1·9%), but in the oldest group of 153 men, average age 56·9 and 16·7 average years of work, the number of cases was 46 (32·2%). This percentage of 32·2% in 153 men was compared with 9·5% of cases in 379 persons of average age of 73·4 years in homes for old people and the difference was shown to be statistically significant. In a discussion of some of the theories of causation of the contracture the opinion is expressed that in the beer wagon drivers it is the frequent and heavy pressure on the palms of the hands of the hundreds of heavy cases of beer which the men have daily to lift and carry which causes the contracture.

M. E. Delafield

OCCUPATIONAL PHYSIOLOGY

Rodahl, K., Astrand, P. O., Birkhead, N. C., Hettinger, T., Issekutz, B., Jr., Jones, D. M. & Weaver, R. **Physical Work Capacity. A Study of some Children and Young Adults in the United States.** *Arch. Environment. Health.* Chicago. 1961, May, v. 2, No. 5, 499–510, 1 map. [22 refs.]

The purpose of the study here described was to ascertain the capacity for physical work of a sample of children and young adults in Philadelphia. The subjects were 601 students aged from 8 to 18 years from 5 schools, and 111 university students aged 20 to 22 years. In the total sample the proportion of non-whites, 27%, was the same as in the total population of Philadelphia schools in 1958.

For the assessment of the capacity for work 4 tests were used. These were (1) the measurement of maximal oxygen consumption (determined in 126 subjects); (2) the performance of a step test; (3) measurement of the pulse response at fixed levels of work; and (4) the LPI, or work-pulse-index test of Müller. Other tests included the measurement of the strength of the biceps, the O'Connor test of manual dexterity, a test of general co-ordination, and the Kraus-Weber test of muscular fitness.

There was no evidence to suggest any systematic difference between the capacities for work of white and non-white children. Between the results from different schools there were statistically significant differences in body weight, body height, muscle strength and capacity for work, and the differences in work capacity appeared to be due to differences in body weight. Up to the ages of 10 to 12 years there was no appreciable difference between boys and girls with respect to work capacity.

In the boys, maximal oxygen uptake was significantly correlated with muscle strength, pulse response to fixed work loads, and the performances in the work-pulse-index test and the step test; and in the girls the same was true except with respect to the work-pulse-index test. There appeared to be no correlation between the results of the Kraus-Weber test and those of any of the physiological tests used to assess physical fitness or capacity for work. General body co-ordination was significantly correlated with manual dexterity, muscle strength, scores in the step test, and the pulse response to fixed work loads. In none of the performance tests were the results significantly correlated with intelligence quotients.

The results obtained in this study were compared with results reported from Dortmund, Germany, and from Sweden. The general conclusion reached is that there was no marked difference between the figures for

Philadelphia and those for Dortmund, while the Swedish subjects were superior in physical fitness to those of Philadelphia. *Thomas Bedford*

HEREMANS, M. T. & LEYH, P. Réaction de Donaggio et taux des éosinophiles sanguins après l'effort physique effectué aux hautes températures. **[Donaggio's Reaction and Blood Eosinophil Levels After Physical Effort at High Temperatures]** *Rev. Inst. Hyg. des Mines.* Hasselt. 1960, v. 15, No. 4, 135–46, 2 figs. [16 refs.]

The authors have studied the changes in the eosinophil count, in the urinary flow, and in the intensity of DONAGGIO's reaction in the urine [see below] during experiments in which the subjects worked while exposed to high temperatures. The subjects, 16 healthy men aged 22 to 36 years, were members of mine rescue teams, and were accustomed to working in hot surroundings.

There were 3 series of experiments. In the first series, which lasted for 1 hour, the men walked on the level at 4½ km. per hour (2·8 miles per hour) with a rest of 10 minutes in the middle of the spell, and they were exposed to dry-bulb temperatures of 46½° to 47°C. (115·7 to 116·6°F.) with 36°C. (96·8°F.) wet-bulb temperature.

In the second and third series the experiments lasted 2 hours, during which time the subjects scaled and descended a vertical ladder 11 times; then walked on the level for 40 minutes, then ascended and descended an inclined plane for 20 minutes, and finally walked again on the level. This combination called for an energy expenditure similar to that required in rescue operations. In the second series the work was done at a dry-bulb temperature of 43°C. (109·4°F.) and a wet-bulb temperature of 31°C. (87·8°F.). In the third series the temperatures were 22°C. (71·6°F.) dry-bulb and 15°C. (59°F.) wet-bulb. The air speed was 1·2 m. per second (240 ft. per minute).

Physical work carried out at room temperature caused a significant fall in the eosinophil level, and light effort at a high temperature produced a similar fall. There was a more pronounced fall when heavy work was done at a high temperature.

When heavy work was done at a high temperature there was a marked and prolonged decrease in the flow of urine, even though water (½ litre) had been taken before work and water was freely available after work. From an analysis of the results obtained with different combinations of work and temperature it is concluded that the decreased urinary flow was mainly due to the heat.

The magnitude of the Donaggio reaction is measured in "Donaggio Units", and the authors have expressed this (a) in terms of the concentration of Donaggio-active substances in the urine, and (b) in terms of the rate of excretion, *i.e.*, as Donaggio units a minute. In terms of concentration the Donaggio reaction increased markedly as the result of work as well as of exposure to heat, and the combination of heavy work at high temperature produced maximal results. In terms of the rate of excretion of Donaggio-active substances in the urine, the effects of physical effort were evident, but exposure to heat had little or no effect.

[If an appropriate quantity of an aqueous solution of a basic aniline dye is added to urine, and ammonium molybdate is added to this, the normal result is complete precipitation of this dye. In certain conditions the composition of the urine is such that precipitation of the dye is incomplete or obstructed (DONAGGIO, *Boll. Soc. Ital. Biol. Sper.*, 1933, v. 8, 1456).] *Thomas Bedford*

OCCUPATIONAL DISEASES

OCCELLA, E. & HENKING, E. **Researches on Differential Grinding of Rocks and Synthetic Materials in Connection with their Silica Content.** *Med. d. Lavoro.* 1961, Feb., v. 52, No. 2, 81–91, 2 figs. (1 coloured on pl.) [15 refs.]

The products of comminution of rocks and synthetic materials have been found repeatedly to differ significantly from the parent materials in their average composition and their content of free crystalline silica. This is particularly true of atmospheric dusts and the fine fractions of settled dusts (VIGLIANI, *Pact.*, 1955, v. 9, 10; OCCELLA *et al.* (1952) Proc. XVIII Nat. Congress Industr. Med.). The potential hazards of handling different silica-containing materials has been estimated by grinding them under standardized conditions and then finding out the content of "sub-sieve" particles, *e.g.* smaller than 40μ in size, and the proportion of free crystalline silica present in this fraction (LANDWEHR, *Atlas zur Charakteristik der Silicosegefarlichkeit von Gestein und nutzbaren Mineralien deutscher Lagerstätten.* 1947, Essen, Bergbau Berufsgenossenschaft).

The first object of the present study was to investigate whether any correlation existed between the proportion of particles under 40μ and particles under 5μ in the dusts examined and also between the free silica content of the two fractions. An interpretation was also sought of observations made in a previous study by one of the authors [OCCELLA, this *Bulletin*, 1955, v. 30, 776, 777] on the extent of variation it is possible to examine and analyse with present-day techniques in the silica content of very fine particles of certain materials, and the silica percentages were then compared with the average content in the original materials.

It was hoped also to establish criteria which would enable the potential effects of a given material to be predicted. Previously described indices (ARIANO, *I materiali stradali*, 1948, Milan, Gorlich; TALOBRE, *La mécanique des roches*, 1957, Paris, Dunod; GUILLOT, *Le problème du broyage et son évolution*, 1960, Paris,

Eyrolles) of crushing and friability obtained from comminution tests performed under different conditions with standardized methods for each type of test were used in the present research. 23 types of rocks and synthetic materials were chosen for examination so as to represent as comprehensively as possible the raw materials of mines and of the iron and steel industry. Grinding was carried out in such a way as to reproduce the complex mechanical stresses which cause the dusts which arise during common operations such as loading, unloading, drilling, blasting and handling of material. Grading was done with calibrated sieves of the finest dimensions obtainable (about 40μ). Microsieves proved unsatisfactory for finer grades and pneumatic centrifugal separation was needed. The various grades were then analysed by optical examination, chemico-photographic analysis and finally X-ray diffraction to differentiate the various crystalline forms of free silica.

No direct correlation could be demonstrated between the percentage values by weight of particles under 40μ and those under 5μ. There was, however, a relationship between the percentage by weight of particles under 5μ to the total weight (the "dust index") and the percentage of particles under 40μ (the "friability index") multiplied by the trigonometric tangent to the cumulative particle size distribution curve corresponding to the finest fraction in the sieve range (the "index of fineness"). It was noted that fired synthetic materials have a greater potentiality for dust production than rocks of very similar chemical composition, for example between fired silica bricks and quartzites, and between common bricks and argillaceous slates. Texture, compactness, degree of cementation and the consequent elastic properties are much more important factors with regard to friability than the composition of the various materials investigated. It was confirmed that no *a priori* relationship exists between the free silica content in the various dust fractions and the mean content of the original sample. The finest dust particles often contained much lower amounts of free crystalline silica than the medium and coarse fractions; thus the atmospheric dust present in environments where some siliceous materials are subjected to industrial processes may be considered as practically devoid of free silica. The hazard from handling various materials may be assessed theoretically by estimating the concentration of respirable particles and their relative free silica content.

[The text of this interesting and instructive paper is in English. Helpful though it may be to predict the nature of dust produced by any given material, it would be dangerous in practice to rely on theoretical considerations alone.] *G. F. Keatinge*

HUBLET, P. Modification de la technique de mensuration et de comptage des poussières. **[Modification of the Measuring and Counting Technique for Dust]** *Arch. Belges Méd. Sociale, Hyg., Méd. du Travail et Méd. Légale.* 1961, Jan., v. 19, No. 1, 63–8.

For measuring and counting dust particles collected by the thermal precipitator the author uses a microscope in which the eyepiece is replaced by a screen of ground glass. The microscope is also provided with Fresnel refractors which ensure a parallel beam of light. Further, objectives of large aperture make it possible to obtain a very clear image on the ground glass. A transparent scale graduated in 200 divisions is fixed around the periphery of the field, and it can be rotated through 360°. With a magnification of 500 times, one division on the scale represents 2 microns.

With this arrangement dust samples can be evaluated more quickly than with the ordinary microscope. There is a saving of about 25% in the time taken for measuring particles, and of 10% in the time required for counting them. Furthermore, with the modified apparatus the precision of the results obtained is improved to a degree that is statistically highly significant. *Thomas Bedford*

DAWES, J. G., TYE, D. L. & WINDER, G. E. **A Semi-Automatic Handpump for obtaining a Sample of Respirable-Size Airborne Dust.** *Safety in Mines Research Establishment.* [Portobello St., Sheffield, 1.] *Research Rept.* No. 198. 1961, Apr., 33 mimeographed pp., 24 figs. [25 refs.] [3s. 9d.]

In order to control the dust hazard the mining engineer must know which operations produce most of the dust, and he must find what effects changes in working equipment and mining operations have on the dust produced. A hand-operated sampling instrument can be of value in obtaining such information economically. Such an instrument should collect in a short time (say 10 minutes) a sample of dust of respirable size which can be evaluated on the spot. Such an instrument would also be valuable for exploring the spatial variations of a dust cloud.

The British Pneumoconiosis Research Unit [PRU] handpump satisfies these requirements except that it collects airborne dust of all sizes. Yet, if it is used with a suitable type of filter paper, and if the optical density of the stain produced by the dust is correctly interpreted, the measurements obtained are relatively reliable and reproducible.

This paper describes an improved form of handpump, based on the PRU design but fitted with a size-selector so contrived that only dust of respirable size is collected on the filter paper. Some other features of the original handpump have also been redesigned.

The modified handpump is semi-automatic, with a pumping cycle of 6 seconds. The results of tests of the consistency of the pumping period and of the size-selection characteristic of the sytem are presented, and the paper also includes the results of some preliminary tests made in the laboratory and underground.

Thomas Bedford

HODKINSON, J. R. **Filter-Paper Methods of Airborne-Dust Measurement in Coal Mines.** *Ann. Occup. Hyg.* London. 1961, May, v. 3, No. 3, 184–98, 3 figs. [32 refs.]

In 1948 a filter-paper method of measuring concentrations of airborne dust on coal faces by means of a handpump and densitometer was introduced. The author

reviews the various attempts that have been made to improve the method, by developing a new handpump and long-period samplers with particle-size selection, and by evolving the "S-scale" of density of the dust stain which, for black particles larger than 1 micron, is proportional to the total projected area. The calibrating factor relating stain density to the number or weight of particles depends on both the size distribution and the degree of transparency.

Tests of the correlation of these improved methods with the thermal precipitator and the Hexhlet sampler were carried out underground. It was found that the stain density gave only a very rough estimate of the concentration of dust, whether in terms of the number of particles or of weight. The wide variability of the calibration factor could now be accounted for by random instrumental errors of measurement, or by variations in the composition and size distribution of the dust.

On the other hand, in a given dust cloud the reproducibility of the stain-density measurement was better than that of the particle count obtained by the thermal precipitator. Thus the filter-paper method is valuable in allowing large numbers of comparative dust measurements at a given working place to be made economically.

Thomas Bedford

HODKINSON, J. R., LEACH, S. J. & WALKER, G. L. **A Review of Tracer Studies of the Turbulent Mixing of Respirable Dust with the Ventilating Air in Mines.** *Safety in Mines Research Establishment.* [Portobello St., Sheffield, 1.] *Research Rept.* No. 196. 1961, Mar., 29 pp., 10 figs. [24 refs.] [2s. 9d.]

The turbulent diffusion from continuous and pulsed sources of tracer gas, simulating respirable airborne dust, has been studied. In experimental underground roadways radioactive methyl bromide has been used, and in a colliery nitrous oxide was employed as the tracer.

In long, straight unobstructed roadways the airflow resembles that in a rough-walled pipe. The turbulent diffusion pattern is largely independent of air speed and may be predicted from the measured coefficient of resistance of the mine roadway. The transverse diffusion from a continuous point source on the axis is slow, and complete mixing may not be attained until 100 diameters downstream for a smooth roadway, or 30 diameters for a rough one. Minor irregularities may reduce the mixing distance to 20 diameters. Major obstructions, such as right-angle bends or large changes in cross-section, may produce uniform concentrations within 5 or 10 diameters.

On coal faces mixing is slow where the air-flow is regular and mechanical disturbances are slight; but usually the disturbances caused by machines and by men working produce rapid mixing.

Hence if it is desired to measure the dust exposure of a man near to a source of dust in a straight unobstructed roadway serious errors may arise if the sampling instrument is not placed close to him. Fortunately such situations are in the minority. In most situations a satisfactory estimate may be obtained from an instrument placed a few feet downstream of the man.

Thomas Bedford

DELONCLE, Madeleine. Granulométrie photoélectrique des brouillards. **[Photoelectric Measurement of Droplets in Mist]** *Ann. Occup. Hyg.* London. 1961, May, v. 3, No. 3, 154–61, 6 figs. (2 on pl.)

The author describes a rapid method for measuring the sizes of droplets between 4 and 100 microns in diameter, such as occur in fogs and mists. The method is based on the measurement of the light scattered by individual droplets, and it has the advantage of allowing the droplets to remain freely suspended in air during the observations.

Simultaneous measurements of the sizes of droplets were made by the method described and also by means of a cascade impactor, and the size-frequency distributions so obtained were virtually identical.

Thomas Bedford

JONES, C. **Predicting the Dry and Wet Bulb Temperatures of Coal Mine Airflow.** *Ann. Occup. Hyg.* London. 1961, May, v. 3, No. 3, 129–53, 13 figs. [22 refs.]

In the development of the deeper British coal seams there are 3 basic climatic questions to which the mining engineer requires answers. They are (1) what will be the working temperatures? (2) how will man's output of work be affected by such temperatures? and (3) what amelioration, if any, will be required? This paper is primarily concerned with the prediction of air temperatures, but comments are included on the upper limit of temperatures and on the general principles to be adopted when air-conditioning British mines.

There is uncertainty as to what should be regarded as the limiting temperature for the work of the miner, but in the light of the available knowledge the author assumes that the limit will be in the region of 80° to 85°F. effective temperature.

Before a shaft is sunk information is required about the thermal properties of the strata, and the virgin strata temperatures. With such knowledge it is possible to consider the working temperatures that may occur in the airways as they are opened up and developed. As the mine is opened up the first need is to be able to predict the temperatures at the faces of headings as they advance from the newly sunk shaft. Heat transfer and moisture pick-up are discussed, and the effects of moisture and the heat from the strata on the flow of air in roadways are considered.

At the coal face fresh surfaces at or near the virgin strata temperature are continually being exposed, and other factors such as the heat from machines and the use of water for infusion and sprays also contribute to a rapid rise in the effective temperature at the face.

Methods of limiting the rise in temperature in headings and on coal faces are discussed. *Thomas Bedford*

POWELL, M. **Toxic Fumes from shotfiring in Coal Mines.** *Ann. Occup. Hyg.* London. 1961, May, v. 3, No. 3, 162–83. [Numerous refs.]

The paper summarizes published information on the probable effects of fumes produced by shotfiring in

mines. The main toxic products of detonation are probably carbon monoxide and the oxides of nitrogen. Concentrations of these gases reported by various workers are summarized in tabular form.

Reference is made to the physiological effects of the oxides of nitrogen, and to the results of the experimental exposure of men and animals to nitrous fumes. The evidence of the effects of low concentrations of nitrous fumes on industrial workers is summarized, and the maximum allowable concentrations that have been proposed by various authorities are mentioned.

Colliery officials who conduct blasting operations are exposed to nitro-glycerin, and to a much less extent to α-TNT, from handling the explosives before firing, as well as to the products of detonation. The possible systemic effects of these substances are mentioned.

It is remarked that the pattern of exposure to toxic fumes in coal-mines varies widely, and the hazard to health cannot be assessed accurately. A pilot project is being considered with the object of obtaining a clearer indication of the levels of concentration of nitrogen dioxide in working places underground.

Thomas Bedford

LONGLEY, M. Y. & BERRY, C. M. **Pulmonary Deposition of Aerosols. Effect of Electrostatic Charging of the Animal Body and the Aerosol.** *Arch. Environment. Health.* Chicago. 1961, May, v. 2, No. 5, 535–43, 7 figs.

Previous experiments [LONGLEY, this *Bulletin,* 1960, v. 35, 1173] showed that charging an animal to a high voltage slightly decreased the amount of an aerosol of potassium chromate which was retained in its lungs. These are here extended to include the effect of charges on the particles.

Mice, contained in pyrex glass tubes with only the nose protruding, were charged through the tail to potentials varying between 3 and 13,000 (+ or −) volts. They were exposed to aerosols of chromium compounds having particles around 0·3 μ radius or diameter [the word "size" is used]. After exposure for an unspecified time up to 3 mgm. of aerosol was removed from the lungs. The aerosols were electrified by passing over a fine charged wire and the net charge distribution (positive, negative and neutral) found for each by drawing it between the charged cylinders followed by a membrane filter and estimating the deposits.

A table of results indicates that aerosols in which most of the particles are charged to the same sign are collected best by animals which are oppositely charged. Presumably this is an effect external to the animal and has nothing to do with the deposition of individual particles in the lung airways with regard to which none of the experimental evidence is relevant.

Graphs purport to relate the difference in potential between the animal and the charged particles to the amount recovered from the lungs. It is not stated how the potential of a particle was measured; this depends on its electrical capacity, that is, on its size and surroundings, neither of which is defined. It is probable, therefore, that the potential referred to is not as stated, but some value associated with the ionizing equipment.

C. N. Davies

COCHRANE, A. L. & HIGGINS, I. T. T., with the assistance of J. THOMAS. **Pulmonary Ventilatory Functions of Coalminers in Various Areas in Relation to the X-Ray Category of Pneumoconiosis.** *Brit. J. Preventive & Social Med.* 1961, Jan., v. 15, No. 1, 1–11, 3 figs. [23 refs.]

Medical evidence is in general agreed that progressive massive fibrosis can cause pulmonary disabilities but there is considerable difference of opinion about simple pneumoconiosis and although the early literature has been well summarized in the past by others a further review is now attempted. The surveys in the Rhondda Fach and Leigh [CARPENTER *et al.*, this *Bulletin*, 1956, v. 31, 1233], that at Staveley [HIGGINS *et al.*, *ibid.*, 1960, v. 35, 964] and a new survey carried out in 1958 in the Rhondda Fach [HIGGINS and COCHRANE, *ibid.*, 1961, v. 36, 737], formed the material on which this paper is based. For purposes of comparison use was made of the two surveys carried out in agricultural areas [HIGGINS, *ibid.*, 1958, v. 33, 238; HIGGINS and COCHRANE, *ibid.*, 1959, v. 34, 238].

Although the materials and methods used in these surveys have all been previously described the relevant points are recapitulated and it is considered that in general the material from the various surveys is entirely comparable. The few sources of inter-area bias which might be held to exist were investigated and the conclusion was reached that any effect they might have on the argument would be negligible. The findings of the various surveys are critically reviewed and it is concluded that there is no sound evidence at present to suggest an association of decreasing ventilatory function with increasing category of simple pneumoconiosis. There appears to be less evidence than was previously thought for believing that men without pneumoconiosis are more disabled from the point of view of ventilatory function than those with simple pneumoconiosis. The existence of regional differences in the ventilatory function of miners and ex-miners seems to be established.

The findings of KADLEC and VYSKOCIL (*Pracov. Lék.*, 1950, v. 2, 348) and a number of other workers, who called attention to the relationship between ventilatory capacity and the number of years of exposure to dust, are compared with those obtained in the British surveys, which form the material on which the present paper is based. Although the results differed somewhat, the phenomena described by Kadlec and Vyskocil and others are regarded as important and worthy of further attention. Differential migration may also be important in this respect. The authors are cautious about blaming bronchitis for regional differences and point out that even when subjects with bronchitis were excluded from the Rhondda and Leigh populations the differences remained, and the same was also true in Staveley. Moreover the high prevalence of bronchitis among miners' wives in the Rhondda Fach also suggests that there are non-industrial causes for the high prevalence of bronchitis there.

There seems to be evidence for some decrease in ventilatory function in elderly miners according to the length of time spent at the coal face. This effect seems to be unrelated to dust retention as seen in the radiograph, or to respiratory symptoms. The balance of

evidence suggests slightly that elderly miners are a little more disabled from the point of view of ventilatory function than they would have been if they had never become miners. *G. F. Keatinge*

MUYSERS, K., SIEHOFF, F., WORTH, G. & GASTHAUS, L. Neuere Ergebnisse atemphysiologischer Untersuchungen von Kohlenbergarbeitern unter Berücksichtigung von Silikose, Bronchitis und Emphysem. I. Mitteilung. Das Verhalten der Gase im arteriellen Blut. **[Respiratory Function Research in Coal-workers with reference to Silicosis, Bronchitis and Emphysema. I. The Behaviour of Gas in Arterial Blood]** *Arch. f. Gewerbepath. u. Gewerbehyg.* 1961, v. 18, No. 4, 358–69.

443 miners and 31 workers not exposed to dust were investigated clinically and radiographically, by spirometry and by blood analysis. 28 of the miners showed no radiographic changes. 119 showed silicosis stage I, 227 stage II and 69 stage III. Those in stages I and II were divided into 6 groups according to whether they had emphysema or bronchitis or both, or not. Very definite standards as regards clinical and spirometric evidence for the diagnosis of emphysema were set up. Bronchitis was accepted as present, on the evidence of auscultation, the presence of sputum and the history. The spirometric tests and the methods of analysis of the arterial blood are given.

The results are presented in 4 Tables. The oxygen saturation, the oxygen pressure and the carbon dioxide pressure are lower in all the miners than in workers of similar age not exposed to dust. In an earlier investigation [WORTH *et al.*, this *Bulletin*, 1960, v. 35, 342] this was also shown and in addition the difference between the results in non-exposed workers and miners without silicosis was greater than the difference in the results in miners without and with silicosis. In the present investigation the values for oxygen saturation and oxygen pressure in miners in the different stages of silicosis did not vary greatly from one another.

It is suggested that dust inhalation through a prolonged, possibly non-specific action damages the bronchopulmonary system, whether silicosis is produced or not. Emphysema and bronchitis have an unfavourable influence on the gases in arterial blood in miners with stage I and II silicosis. Bronchitis seemed to act less favourably than emphysema. The measurement of the oxygen pressure in arterial blood is of special importance in judging the effect of silicosis, of bronchitis and of emphysema on the gas exchange in the lung.

Charles L. Sutherland

KANAGAMI, H., KATSURA, T., SHIROISHI, K., BABA, K. & EBINA, T. **Studies on the Pulmonary Diffusing Capacity by the Carbon Monoxide Breath Holding Technique. I. Normal Subjects.** *Acta Med. Scandinavica.* 1961, May, v. 169, No. 5, 583–94, 8 figs. **II. Patients with Various Pulmonary Diseases.** *Ibid.*, 595–609, 1 fig. [32 refs.]

The authors measured the pulmonary diffusing capacity by the carbon-monoxide breath-holding technique. In the first part of the paper they describe studies of the factors that affect the diffusing capacity (D_{co}) and the reproducibility of measurements, and they report their findings on normal subjects.

In the determination of D_{co} the inspired gas mixture was 10% helium, 20% oxygen and 70% nitrogen, with 0·3% carbon dioxide, and the subject held his breath for 10 seconds. The period of breath-holding was measured from the beginning of inspiration to the beginning of forced expiration.

Although the period of breath-holding was standardized at 10 seconds the effect of holding the breath for different periods from 5 to 60 seconds was studied. There was a definite decrease in the D_{co} as the time for which the breath was held increased. Mean values for 5 subjects were 54·0 cc./minute/mm. Hg at 5 seconds, 39·0 at 10 seconds, 31·4 at 20 seconds and 26·8 at 30 seconds. Other factors that affected the D_{co} were the total alveolar volume, collection time, and exercise, but the reproducibility of D_{co} was high provided that the breath-holding time was 10 seconds and that the total collection time did not exceed 3 seconds.

D_{co} is significantly correlated with body surface area, weight, height and age. From measurements on 39 normal subjects a regression equation is given for the estimation of D_{co} from body surface area, and this is recommended for clinical use.

In the second part the results of studies of 96 patients with various pulmonary diseases are reported.

In patients with bronchial asthma the D_{co} was normal during rest, and it was markedly increased during exercise. On the other hand, in pulmonary emphysema the D_{co} was moderately decreased at rest and increased slightly during exercise. Hence it is suggested that D_{co} may be used to differentiate between asthma and emphysema.

The D_{co} was decreased in cases of lung cancer, markedly when the growth was located in the main or the lobar bronchus, and in the metastatic type the decrease was proportional to the extent of the lesions.

In active pulmonary tuberculosis D_{co} decreased with the extent of the lesions, and in miliary tuberculosis, whether active or healed, there was a moderate decrease. In healed pulmonary tuberculosis D_{co} recovered to the normal value in most cases. *Thomas Bedford*

GROSS, P., WESTRICK, Marian L. & MCNERNEY, J. M. **Autocatalysis of Pulmonary Edema.** *J. Occup. Med.* Chicago. 1961, May, v. 3, No. 5, 258–61, 9 figs.

This is a study of pulmonary oedema produced by irritant air pollutants. In fatalities produced by smog, oedema of the lungs is a common finding in older people with impaired pulmonary reserve. In animals injected intratracheally with suspensions of finely divided dust there is a high mortality from fulminating pulmonary oedema, regardless of the chemical or physical nature of the dust. Experiments were carried out to test the effect of the production of pulmonary oedema in animals with impaired pulmonary reserve and in animals with pneumoconiosis. Rats were injected with mineral oil intrapleurally to reduce the reserve. Another series of

rats were given multiple intratracheal injections of quartz dust and a third series kaolin dust, both over a period of 6 months. All the rats were then given an intraperitoneal injection of ANTU (α-naphthylthiourea). A fourth series of normal rats were given the intraperitoneal injection of ANTU to form a control group. In the normal rats the administration of ANTU produced a mortality of 27%. In the animals receiving the mineral oil or the silica or kaolin dusts the mortality was about 60%.

The histological appearances found in the lungs of the rats receiving silica or kaolin dusts are described and illustrated. The oedema fluid was found predominantly about dust foci which were partially demineralized, and the dust was dispersed throughout the oedema fluid. In the rats injected with kaolin the lung involvement was less extensive than with the animals with quartz so that the mortality in these animals was not due to diminished pulmonary reserve. It was considered that the dust dispersed in the oedema fluid acted in a similar manner to dust injected intratracheally. It was considered also that in the presence of pneumoconiosis or of impaired pulmonary reserve, a relatively small amount of oedema may become an autocatalytic process which may terminate fatally. It is also suggested that this process may be the cause of deaths under inhalation anaesthesia of older patients with emphysema.

Charles L. Sutherland

Gross, P., Westrick, Marian L. & McNerney, J. M. **The Mortality from Sublethal Pulmonary Edema superimposed upon Pneumoconiosis or Atelectasis.** *Amer. Indust. Hyg. Ass. J.* 1961, Apr., v. 22, No. 2, 90–92.

The atelectasis was produced in 90 rats by the injection of 10 ml. mineral oil into the right side of the chest. This oleothorax compressed the lungs and reduced the pulmonary reserve. A method of estimating the degree of pulmonary compression produced by the oleothorax is described. The oleothorax resulted in a 37% reduction in the ratio of the volume of thoracic content over the volume of the thoracic cavity. The LD0 and LD50 of ANTU (alpha-naphthylthiourea) were determined by intraperitoneal injection in groups of stock rats and found to be 6·4 mgm./kgm. and 12·3 mgm./kgm. respectively. 30 of the 90 rats were given 6·4 mgm./kgm. ANTU intraperitoneally, 30 others were given 12·3 mgm./kgm., the remaining 30 served as oleothorax controls. 30 normal rats were given the small dose and 30 other normal rats given the double dose of ANTU to serve as additional controls. Doubling the dose in normal animals more than doubled the mortality rate, but in animals with oleothorax increase of dosage had no effect on mortality rate.

Pulmonary compression more than doubled the mortality rate due to the smaller dose. The amount of oedema fluid in the animals was estimated but very little difference was found in the values in the various groups. A comparable investigation was made in rats by intratracheal injections, at monthly intervals, of quartz dust in one group and kaolin dust in another group. When a total of 150 mgm. had been given, one-half of each group received a small dose of ANTU and the other half double the dose. The result was much the same as in the animals with oleothorax.

The cause of the increase of mortality in rats with a pulmonary handicap over that in normal rats, after the small dose, is discussed. The reason for the failure of the larger dose of ANTU to increase the mortality rate of animals with lung compression or pneumoconiosis is not known. *Charles L. Sutherland*

Garavaglia, C., Polvani, C. & Ubezio, A. L'indagine stratigrafica nelle pneumoconiosi. [**Tomography in the Investigation of Pneumoconiosis**] *Med. d. Lavoro.* 1961, Feb., v. 52, No. 2, 98–126, 27 figs. [Numerous refs.] English summary.

Recent literature on the use of tomography as an aid in the diagnosis of the pneumoconioses is briefly reviewed but a comprehensive series of cases which the authors have selected from the extensive records of the Clinica del Lavoro of the University of Milan forms the main part of the paper.

A large number of films are reproduced to illustrate the various diagnostic points which arose and in many cases standard films and tomograms are represented side by side for comparison to show the shortcomings or advantages of one or the other technique. The authors hope by this method to add something to the general fund of knowledge and on the various diagnostic problems which occur in dealing with pneumoconiosis and certainly the reproductions are unusually clear and show plainly the help which can be gained by the use of tomography as a complementary procedure to the standard X-ray examination. In the view of the authors tomography is practically essential in cases of advanced pneumoconiosis and desirable in many other cases. Thus differentiation between pneumoconiosis and pulmonary tuberculosis is often only possible by this means: it is held for example that the appearance of cavitation due to tuberculosis can be distinguished from that caused by uncomplicated silicosis because the shape of the cavity in the two conditions differs: a tuberculous cavity is round while that occurring in silicosis is often elongated or of an irregular or bizarre pattern. It is pointed out that it is only possible to be sure of the extent and shape of cavities in most cases by tomograms which are also sometimes useful in distinguishing between cavities and emphysematous bullae but the difficulty is not minimized. To quote the authors in rather free translation: "Only the practised eye is capable of assessing the fine shades of morphological differences which enable a diagnostic balance to be struck between emphysema and tuberculosis in the living patient."

But the help given by tomography is not always limited to advanced cases and although in general the typical punctiform appearance of categories *p1* and *p2* are not revealed in the tomogram nevertheless if they are sufficiently numerous to form groups they will be seen as such. And in the case of category *p3* the tomogram may show up nodules of larger size which are hidden in the standard film by the wide dissemination of punctiform shadows: categories type "m" and "n" are also more easily recognized with the help of the tomogram than

in the standard film. The use of tomography in cases of carcinoma superimposed on pneumoconiosis, in the hilar and mediastinal alterations of pneumoconiosis, in the study of distortion of the thoracic organs following pneumoconiosis and of the "middle lobe" syndrome as well as in asbestosis is also well described and illustrated. Hardly anyone will disagree with the authors when they say: "Every time one applies oneself to the reading and interpretation of a series of X-rays of pneumoconiosis one remains struck by the polymorphism of pneumoconiotic lesions: pneumoconiosis presents in fact radiological appearances which simulate the most diverse diseases of the thoracic organs. And often many of these appearances are seen together on an X-ray. Tomography delineates analysis and differentiates forcibly this polymorphism since it does away with the effects of superimposed shadows and the suppression of others which happens so frequently in ordinary pneumoconiosis films". [Abstracter's translation.]

[This is an excellent review and is worth looking over for the illustrations alone.] *G. F. Keatinge*

COCHRANE, A. L., MOORE, F. & THOMAS, J. **The Prognostic Value of Radiological Classification in Cases of Progressive Massive Fibrosis.** *Tubercle.* 1961, Mar., v. 42, No. 1, 64–71, 3 figs. [13 refs.]

The new "International Classification" (Geneva, 1958) of radiographs and pneumoconioses [this *Bulletin*, 1960, v. 35, 21] is largely based on the previous ones and for this reason a great deal has already been validated by evidence that the various categories are related to differences in other biological functions, *e.g.*, pulmonary function and expectation of life. However, the classification of "large opacities" is entirely new and it seems important to see whether this classification could be rapidly validated and in this paper a description is given of an attempt to see whether the three categories of "large opacities" were related to differences in mortality in coal workers' pneumoconiosis in South Wales. Full-size radiographs of all the miners and ex-miners taken during the first Rhondda Fach Survey in 1950–51 [COCHRANE *et al.*, this *Bulletin*, 1953, v. 28, 408] were available and all the radiographs that had ever been previously read as showing simple pneumoconiosis or progressive massive fibrosis were selected and classified according to the new International Classification. In cases of progressive massive fibrosis the outline of the shadow was traced and the area estimated on squared paper. For this work "increased radiographic translucency covering at least one third of one lung field not due to any other cause" was used as a definition of the lower level in "emphysema", and for "distortion" that of the original classification [FLETCHER *et al.*, *ibid.*, 1950, v. 25, 475] was used.

The age-specific mortalities for the three groups A, B and C are shown in a table and in a figure and it is clear that the three categories have very different mortality rates and from this point of view the classification can be considered validated. There is however little excess mortality associated with category A compared with the age-specific mortality for all the non-miners living in the same area over the same period, and the standardized mortality ratio of this group is close to the national average [CARPENTER and COCHRANE, this *Bulletin*, 1956, v. 31, 1015]. By using the additional symbols recommended in the new International Classification such as "em" for marked emphysema, and "di" for distortion of the intra-thoracic organs a table has been constructed to show the observed expected deaths for those interpreted as without emphysema and distortion respectively. The observed deaths were greater than the expected deaths in all three groups of emphysema but did not reach the conventional limits of statistical significance.

In both distortion groups however the observed deaths were less than the expected but again the difference was not significant. It is considered that although it would be wrong to conclude that such symbols are unimportant they are probably less important for prognosis than the main sub-divisions into A, B and C. The background category of simple pneumoconiosis was investigated to see if it had any prognostic value and the results are shown in a table. There is an apparent difference between the mortality of those with category 2 and 3 simple pneumoconiosis associated with category A and between those with an unreadable background and those with categories 2 and 3 associated with category B.

Quick visual assessment of the area involved in progressive massive fibrosis in general gave a fair correlation with actual measurement although errors did occur, thus 7 radiographs originally classified as category B were on measurement found to be less than 5%. It was also clear that if the lower limit of category C had been drawn at one-half instead of one-third of a lung field as was canvassed when the new classification was under discussion, only 8 cases out of 879 of the radiographs examined would have been regarded as falling into it. The area involved by shadows is unexpectedly accurate prognostically and a table showed very clearly the high mortality associated with extensive lesions in young people. No excess mortality—compared with non-miners—was noted on average until an area of 20 sq. cm. was reached and it can be said also that on average one year of life is lost for every increase of 4 sq. cm. in the area of the lesion above 20 sq. cm. Different mortalities associated with different background categories are probably due mainly to differences in the average area involved.

It is concluded that although measurement of the area of the progressive massive fibrosis lesion may be a useful research tool, simple visual assessment is quicker and simpler for routine use. *G. F. Keatinge*

COCHRANE, A. L., MOORE, F. & THOMAS, J. **The Radiographic Progression of Progressive Massive Fibrosis.** *Tubercle.* 1961, Mar., v. 42, No. 1, 72–7.

Every day miners have to be advised, mainly on the basis of their chest radiographs, about the type of work they should do. This cannot be done satisfactorily until more is known about the factors influencing progression of progressive massive fibrosis. It was therefore decided to re-investigate the problem [this *Bulletin*, 1956, v. 31, 1234]. Full-size radiographs were available of all the miners and ex-miners taken during the first Rhondda

Fach Survey [COCHRANE *et al.*, *ibid.*, 1953, v. 28, 408]. This population can be considered as practically unselected as 95% of the miners and ex-miners were examined by X-ray at that time. With this population as a basis an attempt was made to obtain another radiograph of all those whose X-ray of 1950–51 had been read as showing simple pneumoconiosis or progressive massive fibrosis. The radiographs were later classified according to the International Classification [*ibid.*, 1960, v. 35, 21] and later the pairs of radiographs whose first films showed progressive massive fibrosis were read together and a judgment was made whether the progressive massive fibrosis shadow had increased in size. The outline of the shadow was subsequently traced on both first and second films and the area was estimated on squared paper. A complete industrial history and details of some personal characteristics had been obtained at the time of the survey and occupations for the 8-year period of follow-up were classified into dusty and non-dusty occupations and into light and heavy work. Results of the X-ray readings enabled two indices to be used—"the frequency of progression" and "the average increase" in "radiographic area". The latter is subject to considerable observer error but by randomizing the first and second films and concealing dates and names, bias was relatively easily excluded.

A table shows that of 579 X-ray films which were compared an actual decrease was recorded in 48 cases and in one of them a decrease of 70 sq. cm. was noted. Careful re-examination of the films in this instance showed that this decrease was real and it was thought possibly to be due to the closure of a cavity: nevertheless it is held that some of the decreases seen in other cases should be viewed with caution. Another table shows the radiological assessment of changes and the increase in radiographic area of the shadows side by side and it is clear that the quantitative method is the more sensitive of the two.

The number of cases of progressive massive fibrosis recorded at the original survey in 1950–51 was 879 but 33 men had left the area, 15 refused to co-operate and 252 had died and it was felt that this might possibly be a source of bias. For detailed analysis a sub-group in which the selective effect of death would be small was desirable and it has been shown that if the area of shadow is less than 20 sq. cm. no excessive mortality, compared with miners and ex-miners without progressive massive fibrosis, and with non-miners in the same area, is found. This sub-group therefore was chosen for study. Investigation of the importance of age and initial area indicated that both the frequency of progression and the average increase in area increases with initial age. The background category of simple pneumoconiosis and the extent of exposure to occupational dust were also considered in relation to the frequency of progression and average increase in area involved, and it is concluded that the average increase in the dusty group if standardized for initial area will be much greater. Except for the frequency of progression in the younger age-group in general a background of Category 3 is more dangerous than one of Category 2. In view of the many factors involved an analysis of co-variance was carried out and the results are shown in a table; however, only the effects of age reach the conventional standard of significance.

Little practical progress has in fact been made as a result of this investigation but it is suggested that studies of two groups—exposed and not exposed to dust—allocated in a random manner are really required although there are great practical and ethical difficulties in undertaking such a task. In so far as the importance of area suggests some active process on the surface of the mass causing the increase to be proportional to the original area, a biochemical approach appears to be indicated. Meanwhile it seems reasonable to advise miners under 45 with early progressive massive fibrosis to leave mining and learn another trade.

G. F. Keatinge

CENTRAL MINING—RAND MINES GROUP. HEALTH DEPT. **Report for the Year 1960.** [COETZEE, A. M., Chief Medical Officer.] 25 pp., 2 folding charts. 1961. Johannesburg: P.O. Box 1056.

Dr. Coetzee's report gives an idea of the scope of the work of the Health Department of the Rand Mines Group. The department has a staff totalling 629 persons including 18 whole-time doctors. The average number of Africans employed during the year was 82,534: there was a very considerable turnover of labour at the gold-mines. 7 of the gold-mines and one of the other mines in the group had fully equipped hospitals; serious cases were transferred to these hospitals from the sick bays at the other mines. The average stay in hospital per patient was 6·43 days. Africans injured at the gold-mines numbered 19,349, and 136 died. 109 workers were killed outright by accidents: 25 of them by a disaster at one mine. The commonest type of accident was to the hand, the next most common was injury to the leg below the knee. 2·06 shifts per African employed were lost through accidents; and 2·96 for disease. 36,131 patients were treated for various complaints varying from chickenpox to primary carcinoma of the liver. Several diseases are separately considered.

All forms of pneumonia except tuberculosis seem prevalent, especially in new recruits during the first 3 months of service. Meningococcal meningitis did not cause death in the 26 cases. It is interesting that a change similar to that in Great Britain has happened to the tuberculosis of the African in the gold-mines. The death rate is the lowest on record (0·06 per 1,000). The number of new cases has increased because of the use of the miniature X-ray, so that the disease is discovered at a very early stage, and possibly some are incorrectly diagnosed. 75% of cases are discovered while still at work and symptom free, only a quarter have positive sputum. Coetzee raises the point that the present Pneumoconiosis Act leads to these patients being debarred from employment in the mines. The *Report of the Departmental Committee of Enquiry into the Relationship between Pneumoconiosis and Tuberculosis* under the chairmanship of Professor OOSTHUIZEN recommended a procedure involving a delay so that such patients could be investigated and treated and later, if free from tuberculosis, could be allowed to return to the mines. This recommendation was not acted on in the 1956 Act. 98 cases of pneumoconiosis were diagnosed, 60 with accompanying tuberculosis. Scurvy

occurred in 27 patients. Africans are still averse to eating vegetables. The other 4 mines in the group are discussed separately so far as accidents and diseases are concerned.

Hospital costs are given in detail. The average cost per patient per day for 1960 was 18s. 6·2d.

The medical services to the women and children at 3 hospitals and 3 clinics are also mentioned.

[The cost per patient per day for the Modder East mine is given as 42s. 5·2d.; the correct figure is 16s. 3d. (personal communication from the Chief Medical Officer).] *Charles L. Sutherland*

PAUL, R. **Silicosis in Northern Rhodesia Copper Miners.** *Arch. Environment. Health. Chicago.* 1961, Feb., v. 2, No. 2, 96–109, 15 figs.

This is a summary of experience gained, over 12 years, of the classical silicosis of the copper miners of Northern Rhodesia. During that time improvements in dust suppression have resulted in a decline in the incidence of silicosis to 0·8 per 1,000 workers. No case of silicosis has occurred in any worker whose dust exposure was [presumably entirely] " subsequent to 1950 ". Each miner is examined before entry to work in the mines, periodically during his employment and again before discharge. The radiological classification adopted and the technique used are described.

Macroradiography is found not to give any more information than is supplied by conventional methods. Tomography on the other hand allows better assessment of the extent and distribution of the nodulation than the postero-anterior film. The clinical signs of silicosis are indefinite but a full clinical examination should be made. The erythrocyte sedimentation rate is normal in simple silicosis but is almost invariably raised in infective silicosis. Bronchitis has a low incidence and the author found no evidence to suggest that dust alone is an aetiological factor in its development. Cor pulmonale is most infrequent even in cases of massive silicosis. The pathological appearances of silicosis and of its associated tuberculosis are fully described. Estimations of the silicosis and silica content of the lungs were regularly made: they did not show a close correlation with the degree of fibrosis present.

Drillers have the highest incidence of silicosis and develop the disease more quickly than other underground workers, yet they may be exposed to a lesser dust concentration within the range of 0·4 to 7 microns. Drillers work in dust which has been freshly produced: the electron microscope shows that this dust has a larger proportion of particles below the range of the optical microscope. These may be factors in this difference in the incidence of the disease. *Charles L. Sutherland*

PANCHERI, G. Problemi di igiene del lavoro nel traforo del Monte Bianco. **[Occupational Hygiene Problems in the tunnelling of Mont Blanc]** *Rass. Med. Indust.* Rome. 1960, Nov.–Dec., v. 29, No. 6, 413–23, 2 figs. English summary (3 lines).

When the road tunnel under Mont Blanc which is at present under construction is completed, it will be the largest of its kind in the world and direct communication by road between Northern Italy and France will be possible all the year round. In addition the distance to be covered between the two countries will be considerably lessened. The building of the tunnel is taking place more than 4,000 ft. above sea level and this in itself poses problems. Living accommodation has to be provided for the workers and this is not easy at such a height since the terrain is so difficult. Moreover in winter conditions are severe and snowfalls heavy; indeed as the author puts it " the dangers of avalanches are quite other than hypothetical", and for this reason during the first winter's work the hutments had to be moved to a different site.

The problems of ventilation are fully discussed and a detailed description is given of the system in use. Clearly pollution of the atmosphere could not be ignored and the efficiency of the purifier fitted to the exhaust pipes of the various vehicles is checked routinely by suitable detector apparatus. In addition studies on the nature of the products of combustion are regularly undertaken. Ill effects due to imperfect ventilation have in fact been few but have occasionally occurred among excavator drivers. Air-conditioned cabins are available to isolate the workers from the general atmosphere but so far there has been no need to use them.

Much thought was given to the suppression of dust which is produced principally by drilling rock, detonating explosive charges, removing debris and spoil, and by the movement of vehicles and people. All the drilling machines are operated by compressed air which is piped through steel pipes to the job, and water to enable the work to be done wet is laid on in a similar manner. Large amounts of dust are, however, created when charges are blown and although the force of the explosion carries some of the dust away, ventilating fans have also to be used. Another source of dust is the collection of spoil by dumpers but the material is wetted in order to reduce the amount which becomes airborne, and in any case a certain amount of wetting takes place naturally because water continually drips and flows from the roof and walls. Konimeter readings are regularly carried out and frequent chemical analysis of the dust is made. As a result of wet drilling, the presence of water in the workings and good general ventilation, the risk of pneumoconiosis is small. It was estimated by the geologists that the temperature at the point most distant from the entrance would be about 45°C., but in fact it has proved somewhat lower. Nevertheless regular estimations are made to see that the temperature does not exceed a level which is compatible with health. However, air conditioning and cooling as practised elsewhere may possibly be needed. The use of explosives, and falls of material after exploding charges—even some time later—tend to cause accidents and in an effort to guard against falls of materials the roof is protected by a strong metal network until it is possible for it to be replaced by complete enclosure of roof and walls in concrete. When the St. Gothard tunnel was being built, it is stated, 10,000 fatal cases of ankylostomiasis occurred, but not one was reported when the Bologna-Florence railway line was constructed. As a result of this experience strict sanitary hygiene has been enforced, and in addition the workmen were given talks by doctors

of the National Hygiene Service calling their attention to the disease and advising them on the means of avoiding it.

[A most interesting paper. One must congratulate those responsible for the meticulous care which has obviously been taken to safeguard the health of the workers in this great undertaking. Were there really 10,000 fatal cases of ankylostomiasis when the St. Gothard tunnel was being built?] *G. F. Keatinge*

PATERSON, J. F. **Silicosis in Hardrock Miners in Ontario: the Problem and its Prevention.** *Canadian Med. Ass. J.* 1961, Mar. 18, v. 84, No. 11, 594–601, 1 fig. [73 refs.]

The problem of silicosis in Ontario is greatest in the mining of gold and uranium. The number employed in the gold-mines over the years 1926–59 has averaged 12,000 of whom 55% are exposed to dust. The uranium mines started in 1955, and in 1959 employed 12,290 workers.

The Workmen's Compensation Act was amended in 1926 to make silicosis a compensatable disease. Compulsory pre-employment examinations and annual chest radiography for those exposed to dust in mines was introduced in 1928.

Compensation is paid for silicosis and tuberculo-silicosis when it disables a miner and not merely when it causes a shadow on the chest radiograph. Radiological silicosis without disability is not compensatable. We are, however, not given the criteria for the diagnosis of disability.

From 1926 to 1959, 1,372 miners are known to have developed disabling silicosis and from these victims interesting figures are given. The average number of years of dust exposure in Ontario before the appearance of radiological silicosis has increased from 12·5 years in 1926 to 23·7 years in 1959. The average age at which radiological silicosis was first recognized has risen from 39·7 years in 1926 to 58·4 years in 1958. The average age of silicotic miners at death has risen from 44·3 years in 1926 to 67·4 years in 1959. An account is given of the present preventive measures with the comment that failure to reach and maintain the ideal in dust control is a matter of engineering, economics and human nature. From the medical aspect the supervision consists in the removal of the miner who has developed tuberculosis from his dusty occupation. This is attained by the yearly examination. Miners with radiological silicosis are not compulsorily removed from their occupation. Advice, however, may be given a young miner with radiological silicosis or any miner with rapidly developing silicosis to leave mining.

A very full account of the use of aluminium in the prophylaxis and treatment of silicosis is given. No miner who has mined only in Ontario and who has taken aluminium prophylaxis from the time he started mining has developed radiological silicosis up to the end of 1958. Such workers would have had 14 years and 9 months or less of dust exposure: the reports of the Medical Statistics Unit on this subject should be interesting during the next 15–20 years. *Charles L. Sutherland*

KO, Yuang-Ching & LAI, Chun-Lin. **An Observation on the Deaths of Male Adults in Juei-Fang from the Standpoint of Occupational Health.** *J. Formosan Med. Ass.* 1961, Jan. 28, v. 60, No. 1, 76–80.

Juei-Fang is a mining town with a total population of 55,000. The male working population numbers 16,323 and more than half are engaged mostly in metalliferous mines but also in coal-mines. The causes of death in the 988 males who died in 1955–58 were traced and tabulated according to age and cause. The principal causes of death were silicosis and silicosis plus tuberculosis (157), pulmonary tuberculosis (227), asthma and pulmonary emphysema (34), accident and suicide (151), and other diseases (419).

43 of the deaths were due to silicosis and 114 to silicosis and tuberculosis or silicotuberculosis. The older the age-group the lower the proportion of simple silicosis after the age-group 40–49 years.

The death rate from pulmonary tuberculosis was compared with that in 2 non-mining towns. In Juei-Fang it was 1·68 per 1,000 against 0·53 in Su-Lin and 0·65 in An-Tin. More than half the tuberculosis deaths in Juei-Fang occurred in the mining group, one-third in the jobless group and one-seventh in other occupations. Retired or disabled miners are probably placed in the jobless group so it can be concluded that the mining industry is an important cause of the high death rate from pulmonary tuberculosis. Deaths caused by asthma and emphysema numbered 34, mostly in older age-groups. The proportion of deaths from these causes is smaller than in Su-Lin or An-Tin. More than half of the deaths from accident or suicide occurred in the mining group. The men most exposed to danger seemed to be 30–39 years of age.

There can be no dissent from the opinion that there is urgent need for occupational and safety programmes in the mining industries in Juei-Fang.

Charles L. Sutherland

VIGNERON, J. Étude concernant les risques auxquels sont exposés les constructeurs de fours de boulangers. **[Hazards of Workers Engaged in the Construction of Baking Ovens]** *J. Méd. de Bordeaux.* 1961, May, v. 138, No. 5, 638–49.

A detailed description is given of the construction of baking ovens and of the varied conditions to which the workers who build, maintain and repair them are exposed. The temperatures are always high partly because the baker often leaves repair operations until the very last minute and as a result work has to be done while the ovens are still very hot and in fact 3 hours after having drawn the fire and 2½ hours after the bread has been taken out of the oven the temperature varies according to different investigators from 110°C. to 100°C. However, 5–6 hours later it has fallen to a mean level of 60°C. If the heat does not exceed 80°C. it is relatively well tolerated since the humidity is low.

Dust estimations were made with an apparatus "A.R.M. Du Bouchet" with filters of tetrachlor-naphthalene, and it was found that the number of

particles smaller than 3 microns per litre of air ranged from 5 million to 90 million, while the percentage of free silica varied from 5% to 35%. Comparisons are made with the dust levels in other industries and the author cites findings reported by Dervillée *et al.* (*J. Méd. Bordeaux*, 1957, v. 134, 379): for example in foundries and metal works the dust counts varied from 1 to 50 million particles per litre and in the construction of tunnels and other public works the counts were as high as 200 million particles per litre where dynamite was being used. Reference is made to British work giving permissible levels of dustiness in coal-mines at 650,000 and 850,000 particles per litre for anthracite and bituminous pits respectively. A worker appears to be exposed to risk on average for 160 hours per year but fatigue following work in a cramped position, and dry heat bringing about dehydration of the respiratory passages, favour the entry of dust.

Up to the present ill effects have only been found in 2 workers: in the first a routine X-ray film of chest had shown a moderate amount of fine reticulo-nodulation and the appearances remained unchanged in a later radiograph in May, 1959. This man suffered with shortness of breath coming on sooner and lasting longer than in his fellows doing the same sort of work; he has been accepted as a case of early silicosis and has changed his employment. The second worker had an "eczematous" psoriasis following contact with dust in the presence of profuse sweating. Various methods of guarding against heat and dust are discussed and so far as the former is concerned the simplest method would be to make it obligatory for bakers to draw the fires of their ovens at least 24 hours before work is begun. The advantages and the limitations of respirators and breathing apparatus of various kinds are discussed as a means of protecting the respiratory passages against dust.

[Although the account of working conditions and the environmental studies recorded in this paper are of considerable interest, it is hard to judge to what extent the health of the workers is affected since no indication is given of the number of people at risk, or of the number of those examined.] *G. F. Keatinge*

Beckenkamp, H. Silikose bei Feuerungsstein-Schneidern. Vergleichende arbeitsmedizinische Untersuchungen in vier saarländischen Eisenhüttenwerken. [**Silicosis in Furnace Brick Cutters. Comparative Medical Investigations at 4 Saarland Iron Foundries**] *Arch. f. Gewerbepath u. Gewerbehyg.* 1961, v. 18, No. 4, 416–21, 1 fig. [14 refs.]

Examinations of 18 furnace brick cutters at 4 steel works revealed at foundry A 2 men with silicosis out of 3 examined; at foundry B 1 man with silicosis out of 3; at foundry C no silicosis, but 2 men with chronic bronchitis out of 6; and at foundry D no silicosis or chronic bronchitis in the 6 workers examined.

The conditions underlying these varying results are presented as follows: In foundries A and B there were 3 Siemens-Martin ovens lined with silica bricks. In these works the cutting of the brick was a highly specialized job restricted to a few workers. In foundry B the brick was cut in a small confined space. In foundry C the brick was composed of chamotte, the dust of which is not so silicogenic as silica dust but is irritating to the lungs. Owing to the high temperatures required the brick is cut very precisely, thus necessitating more cutting and grinding. In foundry D there was less cutting, the work was carried out in conditions that allowed the dust to be got rid of easily, and more workers divided the work between them.

The type of work and the risk therefore varies from foundry to foundry. The risk is not diminishing because, with increasing demands for higher temperatures, the brick must be better prepared.

The author advises that this work of cutting fire-resisting brick should be spread out over a number of men and also that men over 40 years of age should be employed so that any pneumoconiosis which develops will not reach a stage sufficiently severe for compensation to be needed. *Charles L. Sutherland*

Loeckell, H., Knorr, G., Einbrodt, H. J. & Fitzek, J. Beiträge zur Kenntnis der Chamottelunge. (Klinische, pathologisch-anatomische und physikalisch-chemische Untersuchungen einer durch Quarzchamotte hervorgerufenen Pneumokoniose.) [**Chamotte Pneumoconiosis. Clinical, Pathological and Chemical Investigations of a Pneumoconiosis produced by Quartzchamotte**] *Beiträge z. Silikose-Forschung.* 1961, No. 70, 40 pp., 24 figs. [52 refs.]

This is a very detailed description of a fatal case of pneumoconiosis in a 54-year-old man exposed for 5 years and 8 months to fireclay dust in a glass works. His exposure to dust arose from the sieving of fireclay and the use of this powder in moulding glass.

In 1952, 6 months after he started this work, an X-ray film of his chest showed no changes. In May 1957 he developed pleurisy with effusion, and after the fluid was removed, radiographic examination revealed small nodular opacities distributed in the upper and middle lobes. From this time the disease progressed and the radiological progression is demonstrated by reproductions of films from the first negative film of 1952 to that taken 2½ months before death, showing massive shadows. At no time were tubercle bacilli found in the sputum. He died of right heart failure on 22nd September, 1958. The post mortem revealed that both lungs were contracted and very firm. No massive fibrosis was found but there were numerous small nodules giving the cut surface a granular feeling to the touch. The histology is illustrated by 12 photographs of sections. There is typical silicosis associated with a mixed dust pneumoconiosis in the form of anthracosis and siderosis.

Chemical analyses were made of the dust in the air round the working place, of the dust content of the sputum and of the dust in the lung. The dust of particle size, less than 1 micron, in the air had a total silica content of 63·60%. Radiographic analysis of this dust showed about 35% tridymite, 5% quartz and 3% mullite. The mullite apparently came from the kaolin during the heating of the mould. The dust from the sputum contained much carbon (soot) particles. Mullite was absent: this substance is evidently retained in the lungs. It is

present in the lung dust. In the lung dust the silica content was 3 times higher than in the remaining parts of the lungs. The dust in the fibrotic parts was also finer. Talc was present: this is used in powdering the mould. The silica in the lung dust proved to be amorphous silica; tridymite was not found.

The authors discuss the possible causes of this rapidly developing silicosis. *Charles L. Sutherland*

GROSS, P., WESTRICK, Marian L. & MCNERNEY, J. M. **Experimental Tuberculosilicosis. A Comparison of the Effects produced by some of its Various Pathogenic Components.** *Amer. Rev. Respiratory Dis.* 1961, Apr., v. 83, No. 4, 510–27, 28 figs. [17 refs.]

This investigation is concerned with the nature of the pulmonary diseases produced by dead and living tubercle bacilli and tuberculin as well as by combinations of these organisms with quartz dust and by quartz dust alone. 300 guineapigs were rendered tuberculin positive by means of a subcutaneous injection of living tubercle bacilli of low virulence of the strain used by ZAIDI *et al.* [this *Bulletin*, 1956, v. 31, 543]. The animals were then divided into groups of 30 or 15 and given intratracheal injections by means of a laryngoscopic speculum. The quartz dust used had an iron content of 8 to 9% and was thus incapable of producing silicotic nodules or collagen within the period of observation. The average particle size of the dust was 0·7μ. Some deaths took place from pneumonia, some animals were killed with ether at various intervals for study and all surviving animals were killed with ether at the end of 13 or 14 months. Paraffin sections were cut from the lungs inflated with formalin and stained with haematoxylin and eosin.

An extensive pulmonary consolidation was produced by the iron-coated quartz dust in conjunction with dead tubercle bacilli. This consolidation consisted basically of a chronic accretive interstitial pneumonitis with extensive obliteration of air spaces, collagenous fibrosis, focal necrosis, calcification and cavitation. The same dust in conjunction with tuberculin produced a similar consolidation although there was less collagenous fibrosis, less focal fibrosis and virtually no calcification or cavitation. The pulmonary diseases produced by the combination of iron-coated dust with either living tubercle bacilli, dead bacilli, or merely tuberculin are very similar and differ from one another in minor details only. These differences in relatively minor aspects are considered to be functions of host susceptibility or dosage of pathogenic agents, or both. The ability of dead tubercle bacilli and of tuberculin in conjunction with iron-coated quartz dust to produce pulmonary disease simulating tuberculosilicosis is interpreted to support the thesis of VIGLIANI and PERNIS [*ibid.*, 1959, v. 34, 347] that tuberculosilicosis is basically a reciprocal potentiation of the inflammatory response to quartz dust and to the tuberculous infection.

[An excellent series of microphotographs forms an appendix to this paper and as might be expected the similarity to the appearances in the mixed dust fibrosis as described and illustrated by MCLAUGHLIN and HARDING (*ibid.*, 1957, v. 32, 157) is interesting]. *G. F. Keatinge*

BORNEY, J. Considérations sur un cas de pyopneumopericardite survenu au cours de silicose. **[Pyopneumo-Pericarditis complicating a Case of Silicosis]** *Med. d. Lavoro.* 1961, Feb., v. 52, No. 2, 92–7, 1 fig.

This is a description of the clinical findings in a case of pyopneumopericarditis occurring in an anthracite coal miner aged 34 years. Post-mortem examination confirmed the diagnosis and micro-nodular confluent silicosis was also present. There were, however, no fistulae between the pericardial sac and the broncho-pulmonary tree, and the report is published because the condition is so rare and there appears to be no previous reference in the literature to its occurrence in conjunction with silicosis. *G. F. Keatinge*

MORNEX, R. & MICHAUD, J. L. Le Traitement des signes fonctionnels de L'insuffisance respiratoire silicotique, par myxoedème provoqué à l'iode radio-actif. **[Treatment of Functional Signs of Respiratory Insufficiency in Silicosis by Myxoedema Induced with Radioactive Iodine]** *Arch. Malad. Professionnelles.* Paris. 1961, Jan.–Feb., v. 22, Nos. 1/2, 62–3.

Myxoedema was induced by the administration of radioactive iodine as treatment in a case of advanced silicosis and the clinial details are given. The object was to reduce metabolism and so to relieve the heart. The patient (whose age is not stated) had worked up to 1953 as a maker of electrodes in which refractory material was a component. In 1951 characteristic silicotic lesions had appeared and by 1954 he was regarded as permanently incapacitated to the extent of 100%. Between 1959 and 1960 he was in hospital on 3 occasions as a result of severe respiratory distress. Lung function tests showed the presence of marked respiratory insufficiency and in the electrocardiograph [ECG] the T wave was inverted and there was evidence of right ventricular hypertrophy in limb leads 2 and 3, and in all three limb leads signs of right auricular hypertrophy were present.

30 millicuries of radioactive iodine were given in divided doses at an interval of 3 weeks during February 1960 and by May the shortness of breath had begun to improve. Nevertheless further respiratory function tests and ECG examination carried out at this time gave precisely similar results to those previously obtained. However, in November 1960 the man's condition was so much better that he was able to walk 2 kilometres without undue difficulty. It is pointed out that the improvement in this case was purely functional since lung function tests showed the respiratory insufficiency to be unchanged, while the heart condition was, if anything, rather worse. Although it is difficult to draw conclusions from a single case, the outcome encourages the hope that it may be possible to relieve the functional troubles from which silicotic subjects suffer so severely.

G. F. Keatinge

IRMSCHER, G. & SCHULZ, G. Experimentelle Silikose bei Ratten nach einseitiger Phrenicusexhairese. **[Experimental Silicosis in Rats after Unilateral Excision of the Phrenic Nerve]** *Arch. f. Gewerbepath. u. Gewerbehyg.* 1961, v. 18, No. 4, 422–41, 11 figs. [34 refs.]

This investigation into the effect of excision of the phrenic nerve on the development of silicosis in rats was preceded by two experiments. The first showed that unilateral excision of the phrenic nerve caused an increase of the rate of breathing and a reduction of the volume.

The animals were subjected to a period of stress in a rotating tube: the result was a further decrease in the ventilation of the lungs. In the second experiment the rats were injected intratracheally with coke dust, and then subjected to unilateral phrenic excision. It was found that the longer the rats survived the greater the retention of dust in the affected lung. Phrenic excision delays the elimination of dust *via* the bronchi and, by diminishing the movement of the lungs, it reduces the movement of dust through the lymph channels. The dust in the affected lung remains diffuse while in the healthy lung in time it collects into masses.

In the main experiment silica dust of particle size under 5 microns was injected intratracheally in 2 doses during inspiration. The left phrenic nerve was then excised. The animals were killed 2 at a time at intervals of 4 weeks. After 5 months palpable nodules were found in both lungs but they were smaller in the right lung. The differences between the two lungs increased up to 1 year, when the fibrosis in the left lung had progressed so that only at the apex and at the margins was there any healthy lung The lymph nodes at the bifurcation of the trachea were larger in the left side than on the right. 4 months after the operation the left diaphragm was found to be thinner than the right, and this atrophy increased each month so that eventually the muscle was replaced by connective tissue. The authors note that a small part of the pars costalis of the diaphragm of these rats retained its muscle, evidently this part was supplied by branches of the 12th intercostal nerve.

The histological examination of the lungs after 4 weeks revealed a non-specific reaction to the dust, in the left lung, however, there were granulomata formed of accumulations of cells. 3 and 4 months later these granulomata showed a fine fibrosis. This was limited to the left side. Even after 5 or 6 months there was no fibrotic change in the right lung, while in the left lung many nodules showed central scar tissue. Fibrosis started in the right lung after 7 or 8 months: in the left lung there was now a definite silicotic nodulation. At the end of a year the right lung showed a silicotiç nodulation but in the left lung there were now conglomerate masses. From the 13th month the progress on both sides was equal.

The effect of phrenicotomy is to disturb the elimination of foreign material from the lungs both by way of the bronchi and by the blood stream. There may be other factors, such as stasis in the lesser circulation or alteration in the vegetative innervation of the lung, but these are not of importance. The effect of the reduced elimination of the dust is to speed up the development of the silicosis in the affected lung.

The results of this investigation permit the suggestion that workers who have a diaphragmatic movement impaired by adherent pleura as shown by X-ray examination should not be employed in any silica-risk occupation. Those employed in such an occupation and those suffering from silicosis should be shown a breathing technique designed to improve the movements of the diaphragm.

Charles L. Sutherland

GRUBINA, A. Y., KRAIKO, E. A., MASLENIKOVA, E. M., RAZUMOV, M. I., SERGEEVA, M. A., SKIRKO, B. K. & SHISHOVA, O. A. **[The Effect of Methionine Enriched Nutrition on the Development of Experimental Silicosis in White Rats]** *Voprosy Pitaniya.* Moscow. 1961, v. 20, No. 3, 41–6, 2 figs. [12 refs.] [In Russian.] English summary.

Recent studies have shown the deleterious effect of a protein-deficient diet on the progress of silicosis. Other studies have established the beneficial effect of methionine on protein metabolism. This paper therefore reports a study, in white rats, of the effect of different amounts of methionine supplement to a diet on growth, metabolism of vitamins C and B2, protein and lipid fractions of the blood serum, the activities of certain enzymes connected with histidine and on the development of silicotic process in the lungs.

Silicosis was produced by the introduction of "industrial dust" containing 92% free SiO_2 by tracheopuncture. 72 rats, of average weight 250 gm., of the same age, from the same stock, were used. There were 4 groups with silicosis and 4 control groups. The first pair of groups received only the basic diet, the 3 other pairs of groups received supplements of 25, 50 and 100 mgm. of methionine. The experiment lasted 250–275 days. [There is more detail of the method in the article.]

The average daily increase in weight in the first group was of the same order in controls and experimental animals—about 420 mgm. The control group receiving 25 mgm. and 50 mgm. made an average daily gain of about 540 mgm., whereas the experimental group receiving 25 mgm. gained 450 mgm. and those receiving 50 mgm., 500 mgm. Enrichment of the diet with 100 mgm. of methionine caused the control group to gain only 360 mgm., but the experimental group gained 530 mgm.

Riboflavine was estimated in the urine [it is not stated over what period] and in the liver and kidneys, the results can be put in tabular form:—

Vitamin B2 (in μgm.)

		Urine	*Kidney*	*Liver*
1st group	controls	17	15·1	19·7
	experimental	23	12·9	15·8
2nd group	controls	28	—	about 22
	experimental	30	—	
3rd group	controls	23	—	—
	experimental	28	—	—
4th group	controls	21	about 16	about 19
	experimental	25		

Similarly, the results of vitamin C can be put in tabular form:—

		Vitamin C (in mgm.)		
		Urine	*Liver*	*Lung*
1*st group*	controls	0·47	3·56	0·69
	experimental	0·34	2·85	1·66
2*nd group*	controls	0·43	about 3·4	—
	experimental	0·36		1·04
3*rd group*	controls	0·86	about 3·3	—
	experimental	0·63		1·26
4*th group*	controls	0·18	2·14	—
	experimental	0·29	2·39	1·39

With regard to plasma proteins the serum albumin was lower but the serum globulin higher than in the control group. Addition of methionine to the diet affected the A/G ratio in the experimental group but not in the control group, where it was about 1·3. As already noted, silicotic rats on the basic diet showed a ratio of 0·7; with 50 mgm. methionine supplement the ratio was 1·2 and with 100 mgm. "the ratio fell and approached that obtaining with the basic diet".

The results of serum lecithin were:—

	Serum lecithin (mgm.%)		
	1*st group*	3*rd group*	4*th group*
Experimental	120	150	103
Controls	120	160	140

The ratio of serum lecithin to serum cholesterol put in tabular form:—

	Lecithin/Cholesterol		
	1*st group*	3*rd group*	4*th group*
Experimental	1·3	2·5	1·6
Controls	2·0	2·7	1·8

The activity was measured of histidine-decarboxylase in renal tissue and of "histidase" in liver and brain. In rats with silicosis the activities of the enzymes were reduced. With the 50 mgm. methionine diet the activities were raised in the silicotic rats but did not reach the levels in healthy rats.

For histological changes in the lungs the classification of BELT and KING (1945) [this *Bulletin*, 1945, v. 20, 776] was used. On the basic diet, changes corresponded to Stage IV; the collagen content of the left lung was about 30 mgm. In group 2 (25 mgm. of methionine) the changes were of Stage II; the average collagen content of the left lung was 18·8 mgm. In group 3 (50 mgm. of methionine) 4 out of the 9 rats showed Stage II changes and the remainder Stage IV; collagen 21 mgm. In group 4 (100 mgm. of methionine) the silicosis reached Stage IV. Furthermore rats of both experimental groups and control rats in groups 3 and 4 showed fatty dystrophy of the liver ("evidence of methionine toxicity").

It is concluded that the lower doses of methionine (25 and 50 mgm.) appear to provide some beneficial effect.

[The results in this article quote only averages for groups with no indication of the distribution of the readings. It would have been interesting if this study had considered recent thought on the nature of the silicotic process, *e.g.* PERNIS and VIGLIANI, this *Bulletin*, 1961, v. 36, 121.] *W. R. Lee*

SAKULA, A. **Pneumoconiosis due to Fuller's Earth.** *Thorax.* 1961, June, v. 16, No. 2, 176–9, 4 figs.

This is an account of 2 patients with pneumoconiosis due to fuller's earth. Both patients had had many years of exposure to dust and had respiratory symptoms. The radiological picture was one of nodular mottling. In one case a post mortem was obtained. The histological findings were similar to those found in the case described by CAMPBELL and GLOYNE in 1942 [this *Bulletin*, 1942, v. 17, 381]. There were collections of macrophages containing brownish pigment. Reticular fibres formed the background of these nodules. The picture was quite unlike that of silicosis. X-ray diffraction studies showed lines characteristic of montmorillonite and one line corresponding to feldspar. Electron diffraction studies produced a pattern coresponding to montmorillonite and excluded the triple layer minerals, kaolinite, illite and mica.

Fuller's earth is described as an absorbent clay mineral consisting of calcium montmorillonite. Montmorillonite is an aluminium silicate $(Al, Fe, Mg)_4Si_8O_{20}(OH)_4$, in which the relative amounts of Al, Fe and Mg are not fixed. The industrial uses are mentioned. Fuller's earth can give rise to pneumoconiosis but the exposure must be very prolonged. [See also this *Bulletin*, 1955, v. 30, 695.] *Charles L. Sutherland*

WEISS, A. Über das Vorkommen eines innerkristallin quellungsfähigen Silicates in Lungen Silicosekranker. **[A Silicate Capable of Intracrystalline Swelling in the Lungs of Patients with Silicosis]** *Hoppe-Seyler's Ztschr. physiol. Chem.* 1961, v. 324, Nos. 3/6, 153–62, 2 figs. [Refs. in footnotes.]

The English summary appended to the paper is as follows:—

"The lungs of silicosed patients contain a silicate, absent from normal lungs, and capable of intracrystalline, one dimensional swelling. Its swelling properties are lost when ammonium, potassium, rubidium or caesium ions are introduced by ion exchange.

"The sensitivity of its detection by X-ray diffraction patterns is increased by several powers of ten by the introduction of long-chain n-alkylammonium ions."

MOGILEWSKAJA, O. J. Experimentelle Studien über die Wirkung von Staub (Staubgemischen) aus Erzkonzentraten seltener Metalle. **[Experimental Studies of the Action of Dust (Mixtures of Dust) from Ore Concentrates of Rare Metals]** *J. Hyg., Epidemiol., Microbiol. & Immunol.* Prague. 1961, v. 5, No. 1, 103–12, 5 figs. on 3 pls.

The metallic ores under consideration in this paper were those of beryllium, molybdenum and titanium. The effects of the dust of the metals or their oxides had already been studied. The beryllium ore concentrate studied contained aluminium and 10% free silica. The molybdenum concentrate contained 5·5% silica and the titanium concentrate 37% iron oxide and 2·16% silica.

The present experiments were designed to discover if the mixed dusts of the concentrates had a different effect

on the lungs from the action of the dusts of the metals or their oxides. The dust of the ore concentrates in amounts similar to those used in experiments with the metals was injected intratracheally into white rats. Over 90% of the dust used was under 2μ. One half of the rats were killed after 5 months and the remainder after 7 months. All the rats failed to increase in weight to the same extent as control rats. This failure was greatest in the rats receiving beryllium concentrate and least in those receiving titanium concentrate.

The rats receiving beryllium concentrate were all killed after 5 months. On examination the lungs showed a distinct diffuse interstitial process and there were dust granulomata formed of histiocytes, fibroblasts and connective tissue. In lymph nodes were miliary and submiliary nodules formed of epithelioid cells. In the lungs of rats treated with pure beryllium oxide granulomata were found only in places. The lymph nodes showed no miliary nodules.

The action of the molybdenum concentrate (94·5% Mo S) was similar to that of the pure metal. There was more distinct productive interstitial process with later a sclerosis and in the lymph nodes some changes were found.

The titanium concentrate dust produced a less definite diffuse proliferation than the other 2 concentrates and its action on the lymphatic system was less marked. Titanium oxide only produced slight changes and a slight sclerosis after 11 months. Neither a follicular nor a diffuse interstitial process was observed. Iron oxide dust produced insignificant changes.

The action of the dust of ore concentrates on the lungs differs from that of the pure metal or its oxides. This may be the result of the effect of the other components on the metal or because the metal has different properties when combined in the ore. *Charles L. Sutherland*

Otto, H. Über Pneumokoniosen durch Erdfarben, insbesondere über Ockerlungen. [**Pneumoconiosis due to Coloured Earth in particular Ochre Pneumoconiosis**] *Arch. f. Gewerbepath. u. Gewerbehyg.* 1961, v. 18, No. 4, 349–57, 3 figs.

Many of the coloured earths produced and used in industry contain silica in amounts varying from 1·5 to 15% or over. The difficulty of judging the risk is increased because many factories use a number of coloured earths and these may be mixed together in manufacture. A description is given of the colours produced by natural ochres of varying iron and manganese content. An artificial ochre is also produced; it has more or less the same composition as natural ochre but acts differently on the lung. The natural ochres or oolite have a more definitive unity of their components and produce a more definite siderosilicosis; on the other hand the constituents of artificial ochre act individually. There are types of natural ochres which have a high content of silica; others a high content of iron oxides. The first type produces a silicosiderosis, the second a siderosilicosis. The author introduced the term "ochre pneumoconiosis" in 1939 [this *Bulletin*, 1940, v. 15, 468] and prefers it as showing that neither a true iron pneumoconiosis nor a true silicosis is produced.

Two cases which came to post mortem demonstrate the features of ochre pneumoconiosis. It is slow in developing and there may be an exposure of 15 to 27 years before symptoms appear. The ochre particles in the lung are sedimentary rock derivatives and are round, not sharp edged or pointed as are silica particles. The slow development of the disease has been attributed to the presence of iron inhibiting the fibrogenic action of the silica. The characteristic radiograph is shown in the 3 figures. A similar radiographic appearance is found in iron ore miners and in silver finishers in England [McLaughlin, 1960, v. 35, 1172].

Charles L. Sutherland

Stofer, A. R. Lungenschädigungen durch feste und flüssige organische Substanzen. [**Injury to the Lungs by Solid and Liquid Organic Substances**] Reprinted from *Pathologia et Microbiol.* Zurich. 1961, v. 24, 107–39, 7 figs. [114 refs.]

This is a thesis presented for the doctorate degree in the University of Zurich. It consists of a very full account of the literature as well as observations by the author himself. At the end of the paper the conditions described are placed in 3 groups, but many are difficult to classify.

(1) *Organic pneumoconiosis*

A. Lung changes produced by the inhalation and accumulation of insoluble organic substances, with the formation of foreign body granulomata with or without fibrosis. Grain dust pneumoconiosis is fully discussed in the text. Bagassosis has lately been ascribed as due to the mechanical irritation of the bronchioles by fine dust but various views have been put forward as to its pathogenesis. Its position in this group is doubtful.

In cork dust pneumoconiosis, pathological proof of the production of granulomata in man is lacking. A granulomatous condition of the lung was reported by Weller and Crellin [this *Bulletin*, 1953, v. 28, 962] as following the extensive use of paradichlorbenzene (camphor pneumoconiosis).

B. Lung changes due to very slightly soluble fats and oils and organic soluble or insoluble vehicles. Oil pneumonia may result from the inspiration of cod liver oil, castor oil, olive oil, cotton seed oil, vaseline, kerosene or benzene. It occurs when the cough reflex is absent or because of an anaesthetic effect. Defective action of the cilia may be a cause. Many cases occur in children. The symptoms are not characteristic; the oil may be demonstrated in the sputum. Radiological changes can be found. The type and intensity of the tissue reaction depends on the kind of oil and its amount. Water-soluble carrier materials for contrast media for bronchography may cause granulomatous processes if the injection is excessive; the resultant granulomata lie around the remains of cellulose derivatives such as carboxymethylcellulose. Shellac has produced a chronic pneumonia in a furniture manufacturer [*ibid.*, 1945, v. 20, 550].

(2) *Lung affections produced by organic material contaminated with bacteria and moulds*

Farmer's lung is placed under this heading but with a

query. Various views as to its pathogenesis are given. An account of silo-filler's disease is given under the heading of farmer's lung; it is explained that it is due to poisoning by nitrous oxide fumes.

(3) *Allergic and toxic lung diseases*

Byssinosis is fully described. Included in the discussion of byssinosis is the condition of weaver's cough. Mention is made of the cases of weaver's cough associated with tamarind seed powder. [Murray *et al.*, this *Bulletin*, 1957, v. 32, 868]. Paprica lung is an example of a toxic lung condition. Others are mentioned but their causation is doubtful.

Some other conditions are described but for various reasons are not classified. Tobacco dust, wood dust and bone meal dust have not been shown to have any injurious effect. Silicosis has arisen in wood workers using emery cloth containing silica, in polishing wood. In the plastic industry many resins may some day produce lung disease. These resins often have admixtures of other substances: the author quotes one as containing 65% quartz in fine dust. The most important factor in the identification of an organic substance in the lung is a detailed industrial history. Sometimes it is impossible to decide if the organic material found is endogenous or exogenous. *Charles L. Sutherland*

Ritter, J. & Dacquet, J. Dépistage et traitement ambulatoire par voie orale du saturnisme par le versenate de calcium disodique (E.D.T.A.: Ca Na 2). **[Detection of Plumbism and Ambulatory Treatment with Oral Calcium Disodium Versenate]** *Maroc Méd.* 1961, Apr., v. 40, No 431, 377–82, 3 charts.

The results of 4 years' oral treatment in foundry workers in Morocco are shown to be good, and no time was lost from work. This is preceded by an account of the Pb excretion test following intravenous injection of a 10 ml. ampoule of 5% EDTA $CaNa_2$. The test has been carried out at the Institut d'Hygiène at Rabat for 1 year and tables set forth detailed findings in 4 subjects who had no symptoms though 3 had anaemia. Only 1 stippled count was greater than 3 per 1,000 red cells. In practice urinary Pb reached highest levels 3–10 hours after injection. A 24-hour excretion above 0·06 mgm. was regarded as suspicious and injections were repeated for 2 or 3 days; one greater than 0·08 mgm. was considered a certain sign of poisoning. In the 4 examples high levels induced by 2 succeeding days' injections fell next day to pre-test values, approximately 192–528 μgm. per day. Coproporphyrin excretion decreased and when EDTA was repeated became normal in 3 or 4 days.

Treatment consisted of 6 tablets of 0·25 gm. of the EDTA salt in the morning and evening for 4 days, repeated twice after intervals of 5 days. This was done when at the comprehensive 6-month examination the stippled count was higher than 3 per 1,000 red cells. In 11 cases the count was zero in 1 month, in 6 it was 1 a month after treatment and in the remaining 5 it was 2 in about 2 months. Tables and figures show serial results since 1958.

Without going so far as to recommend daily prophylaxis as practised in Moroccan manganese mines, this method of control and treatment, with the urinary test in debatable cases, has prevented episodes of acute Pb poisoning. *M. Patricia Fitzsimons*

Iordanidis, P. Influence du B.A.L. et du Ca EDTA Na_2 sur le taux des hématies ponctuées après l'intoxication plombique subaiguë du cobaye. **[Influence of BAL and of CaEDTA Na_2 on Stippled Counts after Subacute Lead Poisoning in the Guineapig]** *Arch. Malad. Professionelles.* Paris, 1961, Apr.–May, v. 22, Nos. 4/5, 208–16, 3 figs. & 1 diagram. [10 refs.]

This work was done to see whether stippled counts would rise when Pb was mobilized which ought to set in train higher blood Pb concentrations, even if briefly: this would be an index of imperfect chelation. Serial stippled counts are shown in representative groups from the end of 24 days' poisoning until 34 days later. Counts were made on alternate days starting 25 days before poisoning. Methods are described. Atypical results were few and a statistical study was made.

A 1% solution of Pb acetate, 6 mgm. Pb per kgm. was injected intraperitoneally in 10 groups of 2 male and 2 female guineapigs, on alternate days. On the 26th day, when stippled cells ranged from 1,360 to 2,400 per million red cells, intramuscular injections were given on alternate days for 16 days of 20 mgm. Ca EDTA Na, per 100 gm. to 3 groups and of 1·5 mgm BAL per 100 gm. to 3 others. In 2 groups given only 1 injection of Ca EDTA Na_2 or BAL at the end of the poisoning period more frequent counts showed a slight fall in the first 48 hours.

In the 2 untreated control groups counts went on increasing for 20–24 days after poisoning and though they decreased during the remaining 10 days they finished at levels higher than the range mentioned above. There was no surge above this range in the treated animals that was significant. *M. Patricia Fitzsimons*

Greengard, J., Rowley, W., Elam, H. & Perlstein, M. **Lead Encephalopathy in Children. Intravenous Use of Urea in its Management.** *New England J. of Med.* 1961, May 18, v. 264, No. 20, 1027–30. [12 refs.]

This paper contains an account of the management of 42 cases of lead encephalopathy in children, with reference to the possible therapeutic value of urea which has been reported in the literature to have been used for its diuretic properties to reduce intracranial pressure in intracranial neoplasms and also in 1 case of lead encephalopathy.

In this series of 42 patients 30 were treated with urea which was usually administered by intravenous drip in a 4% solution in 5% dextrose in water in dosages of 1 gm. per kgm. of body weight per 24 hours. It is of course necessary to know that urine secretion is adequate before this regimen is undertaken. This therapy usually results in active diuresis over a period up to 8 hours. Other measures, such as the use of calcium disodium edathamil, anticonvulsant drugs, surgical decompression

and supportive therapy were carried out in all cases as indicated.

The results observed in this series are described with tables, and although it is only possible to attempt to classify cases according to their severity, nevertheless the view expressed is that urea is of therapeutic value for "it is our impression that it has a definite and important place in the management of these patients".

There is a good discussion in which it is stated that "The management of acute lead encephalopathy is still not well understood". Deleading measures such as by chelating agents may do more harm than good if used as emergency measures since considerable amounts of lead may be rendered soluble and be absorbed into the soft tissues. Hence the employment of edathamil should be delayed for 12–24 hours while other more active measures are being employed. The experience of the authors of extensive cerebral decompression have been disappointing and it is suggested that refrigeration may prove to be a valuable adjunct in treatment.

Stress is laid in the importance of early diagnosis of lead encephalopathy and on the fact that "Its management must include a variety of therapeutic measures, for no simple approach is uniformly effective".

M. E. Delafield

JONES, A. R., BRIEF, R. S., BENNISON, B. E. & HAUSHEER, W. T. **Evaluating the Hazards of Automobile Gasoline Additives. Recommended Procedures.** *Arch. Environment. Health.* Chicago. 1961, June, v. 2, No. 6, 635–40, 1 fig.

The work described was designed to ensure that a new organic mercury compound added to gasoline should not expose employees, customers or the general public to toxic risks. The authors believe that the guiding principles used may be more widely applicable.

Basically the evaluation of the risks was divided into the same phases as the product development: 1, Experimental; 2, Field Trial; and 3, Commercial. In the first phase, the problem was reduced to a number of specific questions. A tentative maximum allowable concentration was derived from those published for analogous compounds, and in addition the toxicity of the material to animals was tested in various forms and administered by mouth, by the skin and by inhalation. In an "environmental program", whose purpose was to discover the probable risks to people working near where the new material was used, an air sampling method was devised and its efficiency investigated. The output of toxic matter from a car burning treated fuel was measured and the air around vehicles using it was studied. Workers exposed to the material were examined clinically.

The experimental phase gave favourable results, so the investigation proceeded to field trials in which the treated fuel was sold over a limited area. The planning of these trials and the factors influencing them are briefly described. The potential risks were discussed with the local health officials beforehand.

While the experimental and field trials programmes were in progress development work had continued, as a result of which the product was rejected on technical grounds: the authors note very briefly the programme they had proposed for the commercial phase.

This is an interesting description of the interplay of technical and commercial with medical factors in the promotion of a new toxic material. *J. McK. Ellison*

CAVAGNA, G. & FINULLI, M. Effetto pirogeno dello ZnO per via endovenosa. **[Pyrogenic Effect of ZnO Injected Intravenously]** *Med. d. Lavoro.* 1961, Feb., v. 52, No. 2, 127–31, 3 figs. [18 refs.] English summary (9 lines).

PERNIS *et al.* [this *Bulletin*, 1961, v. 36, 334] recently demonstrated the presence in metal fume fever of a circulating pyrogen liberated from leucocytes which had phagocytosed particles of inhaled ZnO. Transmissible endogenous pyrogen had previously been shown to be present in the circulation in numerous febrile conditions such as those caused by streptococci and pneumococci and by the inoculation of endotoxins, viruses or tuberculin, in sensitized animals. This pyrogen is probably similar to that which can be obtained from neutrophil granulocytes (WOOD *et al.*, *Proc. Nat. Acad. Sci.*, 1960, v. 46, 1248). The question therefore arose whether pyrogen would also be found if ZnO were administered intravenously and this possibility has been investigated by the authors.

15 rabbits whose mean weight was 2 kgm. were each given intravenously 50 mgm. of ZnO suspended in 7·5 ml. of isotonic saline solution and in all cases a rise of temperature followed which varied in onset from 45 to 120 minutes. The mean rise was 1°C. and the fever lasted on average 5–6 hours. In 6 rabbits the same amounts of ZnO were given again intravenously 24 hours later: contrary to what had happened after the first injection, in 5 of the animals no rise of temperature occurred thus showing that they had become tolerant to ZnO but in 1 animal tolerance was achieved only after a third injection. These same rabbits which had been made tolerant to ZnO after 24 hours were given serum obtained from donor rabbits which had also been rendered febrile by inoculated ZnO. In all these animals an immediate rise of temperature took place. A white cell count showed a leucopenia 30 minutes after the injection followed about 6 hours later by a considerable leucocytosis lasting for a varying period of time and in some animals it was still present after 24 hours. Thus small particles of ZnO are active whether given by the intravenous route or by inhalation. BURNSTEIN (*Gigiena Truda*, 1925, v. 7, 17) had already demonstrated that this was the case but no distinction was drawn by him between the effects of the metal and its soluble salts. The rapid and conspicuous fall in the circulating white cells is very suggestive of a direct action of the ZnO on the white cells and of the leucocytes as a source of the endogenous pyrogen, since these studies had showed that the pyrogenic effect was not due to the direct action of the zinc.

The whole picture is very similar to the reactions which follow the intravenous injection of influenza virus [this *Bulletin*, 1958, v. 33, 620]. Similar effects have been obtained when substances with large molecules such as dextran are injected and it is probable that other polysaccharides with large molecules act in a similar manner. These substances are capable of agglutinating granulocytes *in vitro* and *in vivo* which suggests an alteration

in capillary permeability and liberation of endogenous pyrogen. *G. F. Keatinge*

KIRCHER, RITTER, MARTI-FECED & BELAOUANE. Symptomatologie neurologique de manganisme. Projet de barème d'invalidités. [**Neurological Symptoms of Manganism. A Scheme for Assessing Disablement**] *Maroc Méd.* 1961, Apr., v. 40, No. 431, 383–8, 5 figs. [16 refs.]

The physical signs of manganese poisoning are regrouped, described in detail and discussed in relation to morbid anatomy and derangement of cerebral function as reported from animal experiments and by neurosurgeons. The clinical picture is essentially one of symmetrical muscular rigidity more or less complicated by tremor and of psychic symptoms, sometimes with pyramidal irritation and vaso-motor, secretory and endocrinological symptoms. Electroencephalographic tracings have been described and show little abnormality except in the fronto-temporal region. Reproductions of X-rays after air encephalography, which was done in 10 disabled patients, show normal ventricles, but evidence of symmetrical frontal atrophy was always found, sometimes in the prefrontal region, sometimes high or low in the fronto-parietal area and never posteriorly either above or below the tentorium. All this seemed to point to the origin of the lesions being in the frontal lobes. The most recent research shows that this localization corresponds more to the reality of events than does earlier work describing affections of the basal ganglia or cerebellum. It is pointed out that even in old patients the cerebrospinal fluid albumin content is markedly increased.

A table shows 4 stages of the disease for assessing disability instead of the usual 3. For the first stage, that of symptoms only, change of work is advised to prevent manganese poisoning; so also for the intermediate stage, when signs appear, and the disability is 1% to 20%. The fully developed stage with neurological signs is rated 20% to 70% and the stage of permanent deformity 70% to 100% with a grant for a third person's help.

No pneumonitis has been observed in these Moroccan miners since 1948 and miniature chest radiography has shown no abnormalities. *M. Patricia Fitzsimons*

TAKEUCHI, T. **A Study on the Industrial Chromium Poisoning (an Experimental Study with ^{51}Cr).** *Osaka City Med. J.* 1960, v. 6, No. 1, 159–76, 9 figs. [23 refs.]

Absorption, distribution, excretion and accumulation of chromium were measured for 10 days after oesophageal or tracheal injection into guineapigs of a solution of potassium chromate containing ^{51}Cr at a rate of 60μc ^{51}Cr per kgm. Urine and faeces were collected every day and each day 1 animal was killed and the tissues ashed. Methods are described, numerous clear figures record radioactivity as counts per minute (c.p.m.) per gm. or per day, and the toxicity of chromium is discussed. The few numerals in brackets below are approximate examples of recorded radioactivity.

Blood concentrations of ^{51}Cr were highest in 1–2 days and after tracheal administration (T) were finally present (100) on the 10th day when the smaller oral (O) amounts had disappeared. Early small values (50) remained in flat and long bones but quickly decreased or disappeared in brain, muscle, teeth, nails and testicle. Liver concentrations after high (1,000) early values decreased; spleen concentrations did the opposite. Final values for stomach and intestine were similar after T and O. Lung values after T fluctuated (5,000 initially, 2,000 finally) and after O were steady (25). A considerable amount (1,000–500) was recorded in the adrenal after T. Kidney values rose after O (5–30) and fell after T (2,000–200).

The descending faecal excretion curve crosses the steady urinary curve (1,000) on the 9th day after O. After T both curves descend close together from high peaks on the 3rd day (final 300). Total excretion was 90·6% of O, 18·7% in urine and 79·8% in faeces, and was 95% of T, 67% in urine and 28% in faeces. After oral and tracheal administration 0·9% and 3·7% respectively remained at the end of the experiments in the administration sites and 0·6% and 1·3% respectively remained absorbed in other tissues.

M. Patricia Fitzsimons

BERLIN, M. & PISCATOR, M. **Blood Volume in Normal and Cadmium-Poisoned Rabbits. A Study over an Observation Period of Three Months, using a Macromolecular Dextran Preparation.** *Arch. Environment. Health.* Chicago. 1961, May, v. 2, No. 5, 576–83, 6 figs. [18 refs.]

The method required by the Stockholm workers had to be sensitive, simple and capable of repetition while not harming the animal or being interfered with by Cd poisoning. Jacobsson's dextran method for determining plasma volume was chosen, tested for reproducibility of results and elimination time, and shown to give results that correlated with those from the Evans blue method, the latter being slightly higher. When corrections were made for elimination times, the dye values were 8% higher than the dextran values, confirming other workers' results from tracer techniques which showed that in the rabbit Evans blue gave values 8% too high for plasma volume.

The mean plasma volume per kgm. body weight for 20 normal rabbits was 36 ml. Half were injected subcutaneously with $CdCl_2$ in isotonic solution containing 1 mgm. Cd per ml., in a dose of 1 mgm. Cd per kgm. daily on 5 days a week for 6 weeks and then one half this dose twice weekly for 6 weeks. These and the 10 controls were intramuscularly injected with 100 mgm. iron on alternate days during the 7th week and then fortnightly. Haematocrit and plasma volumes were determined with dextran in alternate weeks, and also other blood investigations.

In the poisoned group the plasma volume increased. The increase was greater than would be necessary to compensate for the reduced number of erythrocytes, indicating that the reduction is in part due to dilution. After 2 months the group had lost 20% weight; in spite of this there was a rise in total blood volume, but not at this stage more than in controls. Dextran elimination was decreased and therefore the values could not be

ascribed to renal damage causing increased elimination. At this time when hypochromic anaemia had become manifest, 6 animals died. The survivors given the iron showed an improvement in blood values and a reduction in plasma volume and blank values. The last observation is being studied to see if the iron or progressive liver damage was responsible. [See this *Bulletin*, 1961, v. 36, 334].

M. Patricia Fitzsimons

ROZENBERG, P. A. & SMIRNOVA, M. I. **[Radioactive Phosphorus Incorporation into Erythrocytes during Chronic Lead Intoxication]** *Gigiena Truda i Professional'nye Zabolevaniya.* Moscow. 1961, v. 5, No. 5, 35–7. [In Russian.] English summary.

[The English title, published in the Journal and quoted above, is an accurate translation from the Russian and implies passage of ^{32}P into the erythrocytes.]

The introduction mentions that in lead poisoning the normal ratio between haemoglobin iron and plasma iron is altered, the plasma iron being increased. It is argued that this indicates a disturbance of iron interchange and it is reasonable, therefore, to see if other forms of interchange such as phosphorus compounds, are affected in lead poisoning. Briefly, $Na_2H^{32}PO_4$ was added to defibrinated blood. After 2 hours' incubation the sample was centrifuged and the erythrocytes were washed 3 times. After resuspension a sample was taken for erythrocyte and ^{32}P count. 53 patients were investigated, 6 had a mild degree of lead poisoning, 21 a moderate degree and 4 a severe degree, 2 patients had late sequelae. The remaining 20 formed a control group. Ages ranged from 22 to 59 years.

The rate of uptake (incorporation) of ^{32}P of the control group was 6·6–7·8% (other workers quoted found 6–7·5% and 7·5–16·7%). The mild group, who exhibited a small fall in the number of erythrocytes with some basophilic granules and in whom the urinary lead was 2 mgm. per litre during treatment with EDTA, showed a slight reduction of ^{32}P uptake in half the cases and a normal uptake in the others. In 8 (of the 21) moderate cases the uptake was 8–11·5% on admission and 8–9·2% after treatment. In 7 other moderate cases the uptake of radiophosphorus by the erythrocytes was lowered (5·6–6·4%). After treatment this remained lowered (5·6–6·4%). In the remaining 6 members of the moderate group the ^{32}P uptake was normal at 6·7–7·6%. During treatment "the maximum output of lead in urine did not exceed 4 mgm. per litre. In only one patient did it reach 6·25 mgm. per litre". The 4 severely affected patients exhibited severe lead colic and "a steady fall of haemoglobin and erythrocytes". In 2 the uptake of ^{32}P was decreased, 5·4–6·5%, in one it was increased to 9% and in the other it was normal. On treatment with EDTA there was from 0·38 to 6·25 mgm. of lead per litre of urine. In the 2 patients with "residual appearances of lead poisoning" [no details] the ^{32}P uptake was raised, 9·4–9·7%. During treatment the lead in urine was only 0·075 to 0·4 mgm. per litre.

No connexion was found between the ^{32}P uptake and the morphological picture of the blood. It is argued that lead phosphate can affect the permeability of the cell membrane (CLARKSON and KENCH, *Biochem. J.*, 1958, v. 69, 432) and that the persistence of the disturbances observed even after treatment points to the permanent nature of the damage to erythrocytes.

[This paper unfortunately seems to be based on a misinterpretation of Clarkson and Kench (1958) who did not consider permeability of the cell envelope in this connexion, but examined aggregation to the surface of the erythrocytes; see also this *Bulletin*, 1958, v. 33, 764.]

W. R. Lee

REES, K. R. & SPECTOR, W. G. **Reversible Nature of Liver Cell Damage due to Carbon Tetrachloride as demonstrated by the Use of Phenergan.** [Correspondence.] *Nature.* 1961, May 27, v. 190, 821–2.

After prolonging the observation period in rats which were poisoned by CCl_4 and treated at 0 and 6 hours with phenergan, as reported by RECKNAGEL and LITTERIA (*Amer. J. Path.*, 1960, v. 36, 521), the authors continued the antihistamine treatment with successful results. Rats were dosed with 1·25 ml. CCl_4 per kgm., and when phenergan was given, the doses were 25 mgm. per kgm. at 0 hour and subsequently 12·5 mgm. per kgm. In rats treated at 0 and 6 hours there was no significant liberation of hepatic enzymes into the blood for 24 hours and almost no hepatic necrosis, but from then onwards these signs of liver damage appeared and by 48 hours necrosis was similar to that from untreated poisoning. In rats treated at 0, 6, 24 and 30 hours these changes were prevented and were not observed at 72 hours. CCl_4 reaches maximal concentration in the liver in 3 hours and tests with $^{14}CCl_4$ confirmed that it disappears in 24 hours. The treatment did not prevent fatty accumulation in the liver, which in the untreated animal is seen, together with necrosis, at 6 hours.

Since phenergan did not prevent the fatty changes, it cannot act by detoxicating CCl_4. The delayed necrosis after the 2 doses came when CCl_4 was absent. It is suggested that CCl_4 irreversibly damages a reaction that is not immediately essential for the life of the cell since in the presence of phenergan the damage is reversible. One consequence of the primary injury is a secondary disturbance—possibly connected with cellular water and electrolyte movement—which is prevented so long as phenergan is present. Until the vital constituents of this system are re-synthesized, which appears to take 48 hours, the primary injury will continue in force.

[See also this *Bulletin*, 1960, v. 35, 1145.]

M. Patricia Fitzsimons

STEWART, R. D., GAY, H. H., ERLEY, D. S., HAKE, C. L. & SCHAFFER, A. W. **Human Exposure to Tetrachloroethylene Vapor. Relationship of Expired Air and Blood Concentrations to Exposure and Toxicity.** *Arch. Environment. Health.* Chicago. 1961, May, v. 2, No. 5, 516–22, 2 figs. [15 refs.]

The results of 3 controlled exposures to tetrachloroethylene (perchloroethylene) show a means of determining the magnitude of accidental exposure after it has

occurred. Methods are described. In addition to analysing tetrachloroethylene in expired air, blood and urine, physiological responses were tested and serum enzymes measured. A figure shows serial mean concentrations and ranges of the compound in expired air compared with samples taken from a man who lost consciousness during an accident. This man's exposure was repeated by an industrial hygienist protected by respirator.

Groups of 6 volunteers were exposed for 187, 83 and 183 minutes to time weighted average concentrations of 194, 194 and 101 p.p.m. respectively; ranges after the first 12 minutes were respectively 130–244, 170–225 and 73–147 p.p.m. The calculated average exposure during the accident was 393 p.p.m. for 210 minutes.

After the 83-minute exposure the compound was detectable in expired air for 94 hours and after the accident for 400 hours. Decay curves (average concentration in expired air versus time) of similar slope were observed from exposures of similar duration. The average expired concentration was generally proportional to the environmental concentration of similar duration. The length of time the expired compound was measurable (minimum 0·25 p.p.m.) was proportional to both vapour concentration and duration. Individual variation was small. Tetrachloroethylene has a prolonged exponential decay in post-exposure expired air. By analysing a sample within 100 hours after exposure it would be possible to estimate whether the average concentration was more than 200 p.p.m. for 3 hours. The accident data show that it could be measured during 2 weeks afterwards. Exposure should never exceed the MAC of 200 p.p.m. because of rapid light-headedness and incoordination. Blood concentrations rose slowly to equilibrium in 3 hours and the compound was not detectable 30 minutes after exposure. Apart from transient elevation of urinary urobilinogen in 2 subjects previously accidentally overexposed to 1,1,1-trichlorethoane vapour, other investigations were normal. *M. Patricia Fitzsimons*

MONGELLI-SCIANNAMEO, Nicola. Infortunio collettivo da solfuro di etile biclorurato in un gruppo di pescatori. [**Accident from Dichlordiethyl Sulphide in a Group of Fishermen**] *Rass. Med. Indust.* Rome. 1960, Nov.–Dec., v. 29, No. 6, 441–54, 4 figs. [Numerous refs.] English summary.

Relevant literature concerning the effects of dichlordiethyl sulphide is reviewed and attention is called to the quantity of unused chemical projectiles still in existence in European countries [GAFFURI and FELISI, this *Bulletin*, 1958, v. 31, 248]. At the end of the last war many containers filled with mustard gas were thrown into the sea at no great distance from the coast of Italy and one of them fouled the nets of some fishermen in the Bay of Manfredonia on the Adriatic Sea and as a result landed in their boat. After ill-advised attempts to open the container, and also as a result of pressure, a brownish black fluid having a garlic-like smell escaped on to the cover of the container. The fishermen, fearing that the catch might be contaminated, immediately put the container back into the sea but after about five hours all the six men began to experience intense lachrymation, photophobia, irritation of the skin, headache, nausea and cough. The clinical progress of these men is then described. The author feels that similar accidents may well take place again and considers that adequate warning of this possibility and the steps that should be taken in the event of their occurrence should be made known more widely to those likely to be exposed to risk. Instruction should be given on the disposal of containers, methods of personal protection, and simple primary treatment. *G. F. Keatinge*

GLEES, P. Experimentelle Markscheidendegeneration durch Tri-ortho-kresylphosphat und ihre Verhütung durch Cortisonacetat. [**Experimental Myelin Degeneration due to Tri-Orthocresyl Phosphate (TCOP) and its Prevention by Cortisone Acetate**] *Deut. med. Woch.* 1961, June 16, v. 86, No. 24, 1175–8, 1183–4, 1207, 6 figs. on 2 pls. [20 refs.]

This paper contains an account of experiments on chickens to study the toxicology of tri-orthocresyl phosphate. It was found that a single application of 0·1–0·2 ml. of the chemical per kgm. body weight to the comb of the bird caused typical poisoning with considerable constancy. The first symptoms of loss of appetite and abnormal head movements are manifest after 3–4 days and by the 20th day the gait changes from paralysis of the extensors followed in a few days by inability to stand up. Death occurs usually from respiratory failure.

There is a description of the results of the microscopical examination of the nervous system. No histological changes were found in the peripheral nerves but definite, selective degenerative changes (illustrated by photographs) were found in certain tracts of the spinal cord.

Some experiments were also made to study the possible effect of cortisone acetate on the poisoning. It was found that cortisone therapy had a marked influence in lessening the intensity and even preventing the toxic effect. Even if cortisone is withheld until respiratory weakness is present, its administration at that stage may save the life of the bird.

From the results of these experiments it is recommended that in all cases of tri-orthocresyl phosphate poisoning therapy with cortisone should be immediate. *M. E. Delafield*

LINDGREN, S. Å. **A Study of the Effect of Protracted Occupational Exposure to Carbon Monoxide, with special reference to the Occurrence of So-called Chronic Carbon Monoxide Poisoning.** *Acta Med. Scandinavica.* 1961, v. 167, Suppl. 356, 135 pp., 3 figs. & 19 diagrams. [121 refs.]

Because of a parliamentary decision in 1955, the Swedish Workers' Protection Board investigated the

problems of CO poisoning in industry. This able monograph recounts investigations by the medical group on 970 subjects exposed to CO at work—excluding any who had been unconscious for more than half an hour from acute CO poisoning—and on 432 non-exposed controls of similar age, habits and working and sociological backgrounds.

For his purpose, the author started with the assumption that chronic CO poisoning is characterized partly by a symptomatic picture and partly by recordable signs. This was tested by interview and examinations, by taking blood for COHb values from each individual at the beginning, middle and end of the work shift or day at various times during 1956–57, by special investigations in certain groups and by scrutiny of sickness absence rates. The principles of the group investigation technique in the diagnosis of occupational diseases and of the estimation of poisoning risks are described. The work was planned in this way with the co-operation of the British Medical Research Council Statistical Research Unit, after full discussion with those concerned with industry and industrial health and the press. The places chosen for investigation were 5 ironworks, 3 iron mines, 2 gasworks and 3 motor repair shops. Participation by the workers was voluntary.

The principles emerging from the contradictory and incomplete literature on chronic CO poisoning are discussed. In these arguments the Scandinavian authors occupy a central position: their countries had to use producer-gas for internal combustion engines from 1939 to 1945 with a consequent widespread risk of exposure to CO among the general population. Though there is divergence of opinion regarding the frequency of the disorder, they are agreed on its existence. The problem culminated after about 4 years' exposure. However, in their reports, and in the world's literature, studies on conditions of exposure and on the relation between CO absorbed in the blood and clinical manifestations are generally lacking.

As generally understood, chronic poisoning by any substance implies protracted exposure: symptoms may develop slowly or appear suddenly and may be due to cumulation, *i.e.*, transformation or slow excretion and accumulation of increasing amounts as exposure goes on, or to summation of effects. Since cumulation of CO cannot be assumed, to be able to speak of chronic CO poisoning it must be postulated that the effect of CO on a single occasion will cause such change in the organism that it will react differently or more powerfully at the next exposure, so giving rise after a series of exposures to symptoms that did not appear after a single exposure. When tissue hypoxia has reached a certain level, such symptoms as headache, palpitation and dizziness occur —usually at COHb values of 20–30%. When the CO has been expelled and the hypoxia declines, symptoms usually disappear, sometimes after a delay. If tissue hypoxia has been severe or prolonged, there may be permanent sequelae, but this is not the condition implied in the dubious concept of chronic CO poisoning. It is generally described as a disease due to repeated or protracted exposures, or both, to low concentrations that in single instances do not cause any, or only insignificant, symptoms. The symptomatic picture as reported simulates a non-specific neurasthenic syndrome.

Tables and graphs show results for exposed and controls at each work-place as well as for the total and for special groups which are presented according to ascending COHb values. These groups are: (A) non-exposed non-smokers; (B) non-exposed smokers and exposed workers at 1 ironworks, 1 mine, the gasworks and repair shops; (C) exposed workers at the other ironworks and mines; (D) 82 individuals in group C who had a COHb value greater than 7·5%; (E) 14 workers with a relatively high exposure to CO. The results given are: distributions according to age, social conditions, type of shift, length employed, under 2, 2–4 or over 4 years; distributions of COHb values before and at work; frequencies of 11 symptoms and of abnormalities in blood pressure, eye convergence, Romberg test, blood picture and electrocardiogram; mean values of haemoglobin and red blood cells; and sickness rates in age-groups for 10 years. Conditions of exposure are represented in several diagrams. Group E had special eye, ear, blood volume, neurological, psychiatric and electroencephalopathic examinations in hospital. Matched pairs of 60 exposed and 60 non-exposed workers who were referred for psychometric studies are briefly discussed.

At the times of the investigations no workers were absent because of CO poisoning, and labour turnover was not apparently connected with complaints about CO. Those individuals who gave positive answers to the medical history questionnaire were questioned further. Where sickness absence was higher the reasons were not attributable to CO exposure and were probably due to differences in recording.

In Group A, the ideal control group, 25% run the risk of attaining COHb values of more than 4·2%, the maximum value registered being 8%—thus differing from hospital in-patients reported in the literature. The proportion of smokers and non-smokers was the same in exposed and control groups. The only significant difference in symptoms between non-exposed smokers and non-smokers was bad appetite, and between unexposed shift workers and day workers was in the incidence of fatigue. Other variables are discussed, and tables show frequencies of symptoms, complaints and abnormal findings reported in the literature. It was of interest to find that 2 of 3 with abnormal EEG in Group E were found to have had acute CO poisoning in the past.

In the exposed subjects there was an excessive frequency of headache, and this frequency increased with increasing degrees of exposure. This was interpreted by the author as a sign of repeated slight acute poisoning. Among miners some complaints of headache were judged to be due to handling nitroglycerine. The frequency of simultaneously occurring fatigue, headache and dizziness was low in Groups C, D and E and there was no difference in this between controls or among the 3 groups. No other clinical manifestations—which have been regarded as typical of so-called chronic CO poisoning—were more frequent in the exposed than in the controls. The degree of exposure has been judged to be equal to or greater than that of the groups of patients diagnosed to be suffering from chronic CO poisoning reported in modern literature. *M. Patricia Fitzsimons*

WAGNER, W. D., DOBROGORSKI, Olga J. & STOKINGER, H. E. **Antagonistic Action of Oil Mists on Air Pollutants. Effects on Oxidants, Ozone and Nitrogen Dioxide.** *Arch. Environment. Health.* Chicago. 1961, May, v. 2, No. 5, 523–34. [19 refs.]

As well as being present in smog from exhaust fumes, oil mists are associated with hydraulic equipment on jet engines, and with spinning, weaving and crop-spraying. Although these extensive experiments show that in certain circumstances aerosols of some oils reduced the acute lethal effects of O_3 and NO_2, this does not mean that they are recommended for prophylaxis. The oils used were light and heavy mineral oil; standard grade containing the usual inhibitors; detergent, foam, rust and oxidation inhibitors containing motor oil; and additive-free motor oil. Hundreds of mice were used, oil exposures were generally 6- or 4-hour duration, oxidant exposures were based on a CT [concentration in time] value of 3,000 p.p.m-hours for NO_2 and 30 p.p.m.-hours for O_3 in 4 hours, and these values were chosen to produce an approximate LC50 for the particular oxidant. Tables show mortality rates for controls, which inhaled a respiratory irritant only, and for pre-treated and treated animals under the various experimental conditions.

Variables that influenced protection are emphasized, *e.g.*, time and duration of treatment, sequence of oil and oxidant and type of each. The solubility of each gas in oil and the great difference between the partial pressures in the alveoli of O_3 and NO_2 on the one hand and of O_2 and CO_2 on the other are featured in presenting a hypothesis concerning the mechanism of protection. The most effective particle size of the mist was 0·5–1·2 μ; exposure to diatomaceous earth dust, 0·67 μ, gave no protection. Macrophagic mobilization and infiltration in the respiratory tract followed oxidants or oil plus oxidant but not oil alone. Lungs showed phagocytic engulfment of oil mist droplets. Lipid pneumonia was not observed. There was no appreciable difference in the histology after motor or mineral oils.

Protection was significant when either oxidant was given 18 hours after mineral oil. No other combination approached this level. Simultaneous exposure intensified toxicity. Protection after a single oil exposure lasted 8–9 days, it was not dependent on concentration above a minimum, and after repeated oil exposures it decreased. Tolerance to O_3 could be developed later, after protection from pulmonary oedema, indicating incomplete covering of lung surface with the oil film.

M. Patricia Fitzsimons

FREDRIKSSON, T. & BIGELOW, J. K. **Tissue Distribution of P^{32}-Labeled Parathion. Autoradiographic Technique.** *Arch. Environment. Health.* Chicago. 1961, June, v. 2, No. 6, 663–7, 2 figs. [16 refs.]

Male and female mice (7–10 gm.) were injected subcutaneously with ^{32}P-labelled parathion emulsified in 10% ethanol. After ½, 1, 2, 3 and 4 hours the mice were killed by dropping in liquid nitrogen, and radioautographs prepared from 100 μ sagittal sections of the animals.

The subcutaneous deposit was only very slowl absorbed. There was evidence of ^{32}P accumulation i the salivary glands and dorsal brown fat pad but not i the brain. There was activity in the liver and intestin where parathion is known to be converted to paraoxo In the kidney and urinary tract there was activity whic is assumed to be from water-soluble breakdown product

The main finding is that accumulation of ^{32}P do not occur at the sites where cholinesterase is in highe concentration.

[The method does not distinguish parathion or para oxon from their breakdown products, making it difficu to draw any conclusion from these observations. Th quantity of paraoxon needed to inhibit cholinesterase so small that the failure to stain sites containing th enzyme can be understood.] *J. M. Barnes*

CAVANAGH, J. B. & HOLLAND, P. **Localization c Cholinesterases in the Chicken Nervous Syste and the Problem of the Selective Neurotoxicit of Organophosphorous Compounds.** *Brit. Pharmacol. & Chemotherapy.* 1961, June, v. 1 No. 3, 218–30, 6 figs. [23 refs.]

Acetylthiocholine and butyrylthiocholine together wi selective inhibitors were used to study the localization true and pseudo-cholinesterase in the spinal cord ar brain stem of the fowl. The Gömöri technique w used. Comparisons were also made with the rat, guine pig, rabbit and cat.

In the spinal cord and dorsal root ganglia of the he all nerve cells contained true cholinesterase. In the bra stem again all nerve cells contained true cholinestera and some selected tracts also stained. Localization pseudocholinesterase was found in the capsule of th dorsal root ganglia, and some fibres in the cerebellu and choroid plexus.

Birds poisoned with di-isopropylphosphofluorida (DFP) and tri*ortho*cresyl phosphate (TOCP) develop delayed neurotoxic effect. The sites of the neuro damage had previously been identified (CAVANAGH, *Neurol., Neurosurg. Psychiat.*, 1954, v. 17, 163). poisoned birds there was a general loss of staining f pseudocholinesterase but no loss of staining for tr cholinesterase. There was thus no evidence of inhibitio of cholinesterase, more particularly in those ce damaged by these agents.

In the mammals the authors noted that true choline terase was present only in some neurones of the spin cord and brain stem. The distribution of cholinestera in the neurone of the cat, which is sensitive to the neur toxic effect of TOCP, does not differ from that in the r guineapig or rabbit, which are not sensitive.

J. M. Barnes

GERSHON, S. & SHAW, F. H. **Psychiatric Sequelae Chronic Exposure to Organophosphorus Insec cides.** *Lancet.* 1961, June 24, 1371–4. [17 ref

The authors describe phychiatric changes varying fro headache and fatigue to depression and schizophrenia 16 patients who had used organophosphorus (O-

nsecticides for periods of 1½–10 years in Australia. 8 of he patients came from a group of 10 greenhouse technicians. The size of the population from which the other patients were drawn is not given. The authors considered hat there was a causal relationship in their cases between exposure to O-P insecticides and the psychiatric changes. They attempted to extend their observations by a survey n two fruit-growing districts, with inconclusive results. [Insufficient information is given about the degree of exposure of the patients. Episodes of acute poisoning are recorded in some, but these episodes are incompletely documented and no information on the blood cholinesterase activity of most of these patients is given.]. [See BARNES and BIDSTRUP, below.] *H. B. Stoner*

BARNES, J. M.; BIDSTRUP, P. Lesley. **Psychiatric Sequelae of Chronic Exposure to Organophosphorus Insecticides.** [Correspondence.] *Lancet.* 1961, July 8, 102–3.

In the two letters under this heading the authors discuss the previous paper by GERSHON and SHAW [see above] which claimed to have established a connexion between exposure to organophosphorus insecticides and mental illness. Neither of the present writers is in agreement with Gershon and Shaw, and they discuss the shortcomings of those authors' data. Attention is drawn to the absence of psychiatric sequelae to known poisoning by organophosphorus compounds in the much larger and better-documented series of cases from California [this *Bulletin*, 1960, v. 35, 1181] and Japan [NAMBA and HIRAKI, *ibid.*, 1958, v. 33, 768]. *H. B. Stoner*

ANDERSON, D. M. **Treatment of Poisoning by Anticholinesterase Insecticides in the Rat.** *J. Pharmacy & Pharmacol.* London. 1961, July, v. 13, No. 7, 435–42. [11 refs.]

This reports a study of the therapeutic effect of atropine (17·4 mgm./kgm.) and the oximes—pralidoxime iodide (pyridine-2-aldoxime methiodide, P2-AM) or pralidoxime methane sulphonate (pyridine-2-aldoxime methyl methanesulphonate, P2-S) (100 mgm./kgm.)—given separately or together after poisoning by 10 commercially available insecticides.

The insecticides were given to white rats by mouth; therapeutic drugs were injected intraperitoneally immediately afterwards. Further subcutaneous injections were given 4 hours later in some instances. The 10 insecticides included 3 carbamates (isolan, sevin and dimetilan) and 7 organophosphorus compounds. Of these, 4 (phosdrin, gusathion, morphothion and phosphamidon) are dimethyl phosphates and 3 (ethyl gusathion, demeton and thimet) are diethyl phosphates. Atropine and oxime together were never better than atropine alone for insecticides given by mouth, but the combination was better in a single experiment where the insecticide (morphothion) was injected. Oximes seemed of some value with two carbamates, but with one (sevin) oximes aggravated the poisonous effects. Apart from this there was no evidence of harm from oxime therapy even though it might not be of value in treatment of poisoning by some of the insecticides. *J. M. Barnes*

FINULLI, M. & MAGISTRETTI, M. Manifestazioni tossiche antabuse-simili in operai addetti alla fabbricazione di un anticrittogamico di sintesi: il D.T.M.T. (disolfuro di tetrametil-tiourame). [**Antabuse-Like Intoxication in Workmen employed in the Manufacture of the Synthetic Agricultural Chemical T.M.T.D. (Tetramethyl-thiouram Disulphide)**] *Med. d. Lavoro.* 1961, Feb., v. 52, No. 2, 132–7. English summary.

A description is given of the methods used for the production of tetramethylthiouram disulphide which is a synthetic material used as an insecticide and fungicide and also as an accelerant in the vulcanization of rubber. It is known commercially as Thiram or by the initials TMTD. The chemical structure is described and it is pointed out that it is very similar to that of Antabuse or Disulfiram which differs from it only in that 4 ethyl groups are replaced by 4 methyl radicals. Toxic symptoms associated with the use of this substance in vulcanizing processes have been described by WILLIAMS (*J. Amer. Med. Ass.*, 1937, v. 109, 1472) and more recently by MERLEVEDE and ELSKENS (*Arch. Belges. Méd. Sociale Hyg. Méd. du Travail et Méd. Légale*, 1959, v. 17, 237.

3 people engaged in the manufacture of TMTD were admitted to the Clinica del Lavoro suffering from toxic manifestations consisting of general malaise, headache, nausea, flushing of the face and neck, with pruritus and a sense of irritation in the throat with some disturbances of respiration. All the clinical features were aggravated by the ingestion of alcoholic drinks, even those having only a low content of alcohol. Lateral nystagmus was noted in all 3 patients but otherwise investigation was largely negative. Slight abnormalities were observed in the EEG tracings in 2 cases but patch tests were consistently negative and in only one man—an asthmatic—was the lung function as estimated by spirometry considered to be reduced. However 1–2 glasses of wine were sufficient to reproduce the symptoms in all 3 subjects and attention is drawn to the fact that Antabuse gives rise to similar effects.

The explanation may lie in the fact that both TMTD and Antabuse possess a common metabolite—dithiocarbamate—which is an intermediate in the industrial synthesis of the former and has the effect of blocking the hepatic enzyme systems with the result that delayed destruction of acetaldehyde occurs which accordingly accumulates in the blood. However, since the early stages of production of TMTD are fully enclosed and the workers are thus not exposed to dithio-carbamate it has been suggested by Merlevede and Elkens that dimethyl amine—a very volatile gas—and carbon disulphide which are present at the very start of the process when the reactor is being charged, may combine together *in vivo* to form dithio-carbamate. Treatment of intoxication is symptomatic and the condition clears up spontaneously in 2 to 3 weeks. *G. F. Keatinge*

SAMITZ, M. H. **Exfoliative Dermatitis from Exposure to Paint Thinner.** *J. Occup. Med.* Chicago. 1961, July, v. 3, No. 7, 346–7, 1 fig.

MENEGHINI, C. L. & GHISLANDI, E. La profilassi individuale in dermatologia professionale con nuove creme barriera. [**The Prophylactic Use of New Barrier Creams in Occupational Dermatology**] *Med. d. Lavoro.* 1961, Feb., v. 52, No. 2, 144–9. English summary.

The introduction to this paper stresses the importance of industrial dermatitis as an occupational disease and a description is given of the properties of the two principal kinds of barrier cream—the water-repellent and the water-soluble—which are commonly used in the hope of preventing skin irritation at work. The protection which barrier creams can afford and the other merits claimed for them are also discussed. The paper is, however, principally concerned with studies on the efficiency of two new barrier creams, Gantex A which is water-repellent and Gantex O which is water-soluble. These substances differ from other barrier creams since they contain hexachlorophene, vitamin A and silicone in addition to the usual constituents. Various laboratory tests showed that the two creams were reasonably efficient in their respective spheres and similar tests applied to other commercial barrier creams indicated they also were effective to a point.

Clinical trials were also undertaken. The two barrier creams were applied daily for 10–12 days to the skin of 52 healthy subjects and 10 patients suffering from various kinds of dermatoses, *e.g.*, psoriasis and eczema. No alteration in the *p*H was noted and no irritation of the skin occurred in either of the two groups. After the healthy skin of 32 subjects was abraded with glass paper and previously defatted with a solvent and then submitted to moist heat each of the two barrier creams was applied to the skin 2–4 times a day for 2 weeks but without producing any evidence of sensitization. The two barrier creams were applied daily for a week to the skin of 15 patients suffering with pyodermatitis and improvement followed. This did not occur when barrier creams which did not contain hexachlorophene were used. 250 workers in several departments of a large chemical works who were exposed to numerous irritating substances in aqueous solution used Gantex A daily on starting work for 2 months. The workers found that the cream was easily applied, did not render the tasks undertaken by the operator any more difficult and enabled the skin to be cleaned more readily at the end of the shift. No irritation or sensitization of the skin took place and no case of occupational dermatitis occurred during the period of observation although previously some cases had been reported among the workers in each department. 40 operatives engaged in assembly work in a large motor car factory who were exposed to contact with various mineral oils, solvents and varnishes used Gantex O for a month applying it to the skin twice a day. No irritation or sensitization followed its use and no case of occupational dermatitis arose. Before the use of Gantex O some cases of folliculitis had been reported in the department.

The authors feel that the addition of antiseptics and epithelial protecting substances has enabled barrier creams to be used with good effect even in cases of early skin irritation without in any way modifying their ability to give mechanical protection which lasts throughout th duration of a shift.

[Many authorities at the present time are sceptic about the merits of barrier creams and both prima irritation and sensitization of the skin have be attributed to them. Although the barrier creams whi are the subject of the present study have not been fou to give rise to ill effects and were apparently in oth respects satisfactory, these conclusions would ha carried greater conviction if they had been based c trials of a larger number of workers for a greater leng of time and had included adequate controls.]

G. F. Keatinge

WORLD HEALTH ORGANIZATION. PUB. HEALTH PAPE No. 6. **Ionizing Radiation and Health** [LINDEL B. & DOBSON, R. L.]. 81 pp., 2 figs. [55 ref 1961. Geneva: Palais des Nations. [Sales age for U.K., H.M. Stationery Office.] [5s.; $1.0 Sw.fr. 3.–.]

A great deal of the material contained in this repo is taken from the 1958 report of the United Natio Scientific Committee on the Effects of Atomic Radiati and the 1957 report of the International Commission Radiological Protection, but there is a good deal of oth information gleaned the world over which will be of l less interest to the reader who wishes to keep abreast modern methods and views about how to deal wi unwanted radiation.

Dealing first with some of the important biologic effects of radiation, the authors pass on to the physic basis of the requisite measurements that ensure safe and then discuss the various fields of radiation to whi man is subject, *viz.*, natural radiation, modified natu radiation, medical exposure, occupational exposu radio-active fallout, which is apparently still with us.

There is a very useful glossary of technical term The life of a new unit in Physics is reckoned a long o for a great deal of work is put into its establishment b occasionally there is one unit too many. The RE (roentgen equivalent physical) has had a short life; it w a unit of absorbed dose of radiation. The unit now us is the RAD (1 rad = 100 ergs per gm.).

A short but vital section entitled "Comment" (p 63–65) gives the results from a world-wide scrutiny leukaemia, ranging for some countries from 1940 1956.

The most striking feature of these death-rates is t variation in rates from country to country. Taking t death-rate as the number of deaths per million of t population we find an extraordinary resemblance betwe Canada and England and Wales, 52 all in 1956, the ra of rise since 1940 being very similar. On the contra France gives a rise from 18 to 58 since the year 19 Japan has the figure 24 to date while Denmark burdened with a death-rate of 74; the rate having ris gradually from 48 in 1940.

Here indeed is a field of investigation. WHO, whi sponsors this valuable handbook, will doubtless ha more to tell us about leukaemia in the near future.

S. Russ

Food and Nutrition

The order in this section is:—**General; Foodstuffs; Food Poisoning.**

GENERAL

INTERNATIONAL CONGRESS ON NUTRITION. **Proceedings of the Fifth International Congress on Nutrition, Washington, D.C., September 1–7, 1960.** *Federation Proc.* Wash. 1961, Mar., v. 20, No. 1, Pt. 3, Suppl. No. 7, pp. v + 415, illustrated. [Numerous refs.]

The fifth International Congress on Nutrition was held in Washington D.C. on September 1–7, 1960. President EISENHOWER, who gave the opening address, remarked on the wide international representation at the Congress. Members came from 59 countries and from each of the continents. This was reflected in the 7 panel meetings and the symposium reported in the Proceedings, which include contributions from most parts of the world and cover many of the major nutritional problems, ranging from those caused by undernutrition in the poorer countries to the effects of overnutrition in highly developed societies.

The subjects of the panel meetings were:

(1) *Evaluation of nutritional status in man,* pp. 9–57.
(2) *Proteins and amino acids in nutrition,* pp. 61–111.
(3) *Lipids in health and disease,* pp. 115–161.
(4) *Nutrition in maternal and infant feeding,* pp. 165–205.
(5) *Effects of processing and additives on food,* pp. 209–256.
(6) *Animal nutrition and food production,* pp. 261–313.
(7) *Three hours around the world: new possibilities in nutrition research,* pp. 317–261.

A symposium on *World Food Needs and Food Resources* (pp. 365–415) was held on the last day.

Panel 1 was opened by E. W. MCHENRY who spoke on *The interpretation of nutritional requirements in action programmes* (pp. 9–10), pointing out the pitfalls due to uncritical acceptance of standard requirement figures. The papers which followed dealt with the organization of surveys, and clinical, public health, dietary and biochemical means of assessing nutritional status. In summing up the papers in this panel Miss A. M. COPPING (p. 57) emphasized the relative limitations of any one of these approaches and the need for co-ordinating them for accurate assessment.

Contributions to the discussion on *Proteins and amino acids in nutrition* (panel 2) included accounts of the present knowledge on protein metabolism and requirements, papers on protein malnutrition and on the solution of the problem of world shortage of protein, a subject which was singled out for special discussion. Speakers agreed that the sources of food proteins, whether animal, vegetable or synthetic, were unimportant as long as the amino acid pattern of the food was satisfactory. In this connexion J. B. ALLISON's paper on *The ideal amino-gram* (pp. 66–72) was especially relevant. In it he drew attention to the importance of protein digestibility and to the fact that different physiological and pathological states might require unusual amino acid patterns.

Two of the papers presented on the subject of *Lipids in health and disease* (panel 3) dealt with the relation of dietary fats to arteriosclerosis. The remainder were reviews of different aspects of the absorption and metabolism of lipids, including the metabolism of bile acids. This subject is of particular interest since the synthesis of bile acids is closely correlated with the turnover of cholesterol. S. BERGSTRÖM'S review (pp. 121–126) included descriptions of his own work on the influence of the intestinal flora on this process and interesting suggestions as to the possible role of dietary fats in the elimination of cholesterol.

Most of the contributors to panel 4 on maternal and infant nutrition were agreed that the reduced efficiency of lactation, which seemed inevitably concomitant with rising standards of living, was unfortunate, and that breast feeding needed to be encouraged. Nutrition was only one of several factors thought to be important to lactation, and there was some disagreement on the extent of the influence of nutrition. G. GOPALAN and B. BELAVADI (pp. 177–184) showed that poor nutrition tended to reduce total milk output in Indian mothers without apparently reducing the concentration of protein. On the other hand, B. S. PLATT (pp. 188–195) had found changes in the ratio of curd to whey in the milk from poorly fed mothers and thought this an indication of changes in protein quality. In summing up D. B. JELLIFFE (pp. 205–206) stressed the need for further research on the nutritional requirements of mothers and infants.

The general conclusions of panel 5 were that modern methods of processing and most of the additives currently in use had little adverse effect on the quality and safety of foods. Most processed milks had protein of good quality. No ill-effects have yet been found to ensue from the use of pesticides and other agricultural chemicals, nor has the consumption of old-fashioned spices and flavourings shown any relation to the incidence of peptic ulcers or cancer, whereas the palatability and preservation of food was greatly enhanced by all these means.

Panel 6, headed *Animal nutrition and food production,* covered different conditions for promoting the production of livestock. While most of the papers were based on work done in highly-developed countries, much of the discussion was concerned with the problems of livestock production in under-developed regions. K. L. BAXTER concluded his summary (p. 313) of the discussion with a reminder that it was necessary to raise welfare and educational standards in these territories before they could be expected to solve their specific problems.

The subject for panel 7 was *New possibilities in nutrition research.* Most of the problems that were described have been known for some time but are still largely

unsolved. There were accounts of renal calculus disease of the urinary tract, nutrition and physique of Bantu communities, the malabsorption syndrome, neuromuscular disease, and the nutritional aspects of cirrhosis and carcinoma of the liver. As W. H. GRIFFITH (p. 361) summed up, little is yet known of the extent to which nutrition affects various states of ill-health and of how its effects are interrelated with other causes of disease.

A symposium of *World food needs and food resources* was held on the last day of the congress. C. G. KING (p. 365) gave the opening address in which he pointed out how much had been achieved in some countries but also stressed the ever-increasing needs in other parts of the world. He was followed by J. BONNER who, in his paper entitled *The world's increasing population* (pp. 369–372), gave a frightening description of future populations if the present rate of increase were to continue u checked. The next paper, *Prospective world productic and distribution of food* by B. T. SHAW (pp. 373–37 somewhat allayed the preceding horror by taking a optimistic view of possibilities of harnessing the world natural and scientific resources to feed the people might produce. Other contributions dealt with specif aspects of the problem: prospective world productic and distribution of food, water resources, socio-econom factors that limit food production and consumptio pressing nutritional problems of today, and the prospec of meeting protein needs. The closing address was give by M. G. CANDAU (pp. 403–406) who described the pr gramme of the World Health Organisation and its futu plans which include an extension of aid to nutritic research.

Ruth Schwartz

FOODSTUFFS

SYLVESTER, P. K. & GREEN, J. **The Incidence of Heat-Resistant *Clostridium welchii* in some Raw Meat Supplies.** *Med. Officer.* 1961, May 19, v. 105, No. 20, 289–90.

713 samples from 405 carcasses were examined for heat-resistant strains of *Cl. welchii* after steaming; 319 carcasses were sampled at butchers' establishments under contract to provide meat to the Schools Meals Service. 2 samples, 1 from an exposed surface and 1 from a freshly cut surface were taken from each of 300 carcasses, 1 sample each from 19. 50% of samples were taken from jointed and boned meat and 50% from whole joints before boning. 78 samples were taken from freshly killed abattoir carcasses 2 and 30 hours after slaughter; 22 positive results were obtained. 28% of all carcasses sampled at the butchers' establishments were positive for *Cl. welchii*; home-killed meat showed consistently higher positive results than imported meat. English pork showed a higher percentage of positive results than any other type of meat (49% retail, 21% carcass). Samples taken from meat which had been boned and cut, yielded 3 times as many positives as those taken from whole joints. Twice as many positive samples were obtained from exposed surfaces of pork as from freshly cut surfaces. Similar results were obtained from imported mutton and English beef. It is suggested that increased handling of a carcass during boning, etc., will spread contamination. The results suggest that infection is found more often on the surfaces of joints or carcasses than within the tissue substance.

[See also this *Bulletin*, 1961, v. 36, 877.]

Betty C. Hobbs

KERELUK, K. & GUNDERSON, M. F. **Survival of Bacteria in Artificially Contaminated Frozen Meat Pies after Baking.** *Applied Microbiol.* Baltimore. 1961, Jan., v. 9, No. 1, 6–10.

50 ml. of 24-hour cultures of *Escherichia coli, Staphylococcus aureus, Bacillus subtilis,* and *Streptococcus faecalis* were inoculated into chicken meat pies made the laboratory and before they were frozen in a wir tunnel.

Control samples were taken before cooking; pies eac contaminated with a single species were baked for 2 30 and 40 minutes in a gas-oven preheated to 425°F.

Counts were carried out immediately after baking ar again after 10 and 20 minutes. After 425°F. for 4 minutes there was a 0·0002 to 0·1% survival of the no sporeforming bacteria, 0·1% survival of *Strep. faeca* and 0·35% survival of *B. subtilis*. After 30 minutes 425°F. there was a 0 to 3·6% survival of the no sporeforming organisms and *Strep. faecalis* was found the greatest numbers.

After 20 minutes baking 14 to 100% of non-sporin organisms survived and the numbers of *B. subtilis* ha increased indicating multiplication; pies baked for 2 minutes were unpalatable through undercooking.

The internal temperatures in the centre of the me pies at the different baking times were 120°F. for 2 minutes, 170°F. for 30 minutes, and 214°F. for 4 minutes baking, thermocouples were used.

Bacteriological techniques are given.

Betty C. Hobbs

HARTMAN, P. A. & HUNTSBERGER, D. V. **Influence Subtle Differences in Plating Procedure on Ba terial Counts of Prepared Frozen Food** *Applied Microbiol.* Baltimore. 1961, Jan., v. No. 1, 32–8. [29 refs.]

Using frozen chicken pies for bacterial counts inves gations were made on methods of sample preparatic effect of sample size, size of initial dilution, mode addition of initial diluent and type of diluent, duratic of homogenization, time of plating after homogenizatic use of beads, and types of blender; other variables we also studied.

The method of sample preparation was accepted fro previous reports as best carried out by homogenizatic a 50 gm. sample was most convenient and weighed c

into a blender container. Plates usually counted were as dilutions of 1/20, 1/50 and 1/100 for all colonies, and 1/2, 1/5 and 1/10 for the enterococcal count. There was no difference in the results whether the diluent was added in 2 stages, or all at once in the beginning.

Some foods could be blended in 30 seconds to 1 minute, others required more than 2 minutes; samples should be plated as soon as possible after homogenization. Counts were similar from phosphate buffer and 0·01% peptone but they were appreciably lower in distilled water. The use of beads made very little difference, and 5 times shaking only was considered necessary. Differences among blender units were not significant, but the Waring containers were most convenient to manipulate; no significant difference was found in the use of old and new containers.

The results were subjected to statistical analyses and discussed in the light of their effect on plate counts of frozen foods. *Betty C. Hobbs*

THATCHER, F. S. & LOIT, A. **Comparative Microflora of Chlortetracycline-Treated and Nontreated Poultry with special reference to Public Health Aspects.** *Applied Microbiol.* Baltimore. 1961, Jan., v. 9, No. 1, 39–45. [17 refs.]

Commercial chickens of broiler size as eviscerated carcasses in polyethylene bags or as tray-packed "cut-up" poultry meat were purchased from several retail stores in each of 3 widely separated cities receiving poultry from different areas in Canada.

100 each of specimens treated with chlortetracycline (CTC), or untreated were obtained over a period of several months to include various seasonal temperatures and to allow representative sampling. Each specimen was divided equally by aseptic methods; one half was examined immediately, the second half was stored at 5° to 7°C. for 5 days, repulsive odours and surface slime were often found among the stored specimens.

500 gm. from each halved specimen were added to 500 ml. of sterile distilled water in a sterile screw-capped Waring blender vessel and shaken vigorously for 10 minutes in a mechanical shaker. Dilutions were made for inoculation of media.

Mesophilic, pyschrophilic, coliform, staphylococcal, enterococcal and yeast, plate counts were made on selective media. Fluid enrichment cultures for salmonellae were prepared from centrifuged poultry wash water in selenite F plus cystine incubated for 18 hours at 37°C., and sub-cultured on to Kauffmann brilliant green, bismuth sulphite and SS Difco agars. Triple-sugar-iron and urea agars were used for suspicious colonies followed by the usual serological tests.

Sensitivity to CTC of all salmonellae and staphylococci isolated was determined. In addition resistance to CTC of mesophilic and psychrophilic bacteria and yeasts was estimated by duplicate count plates containing 7 p.p.m. CTC in the respective media.

Colonies representing numerically dominant bacteria were tested by the tube method for antibiotic sensitivity. CTC treatment was associated with a higher proportion of resistant enterococci and *E. coli* and with an increased level of resistance among both organisms, although there was no significant change in the numerical prevalence of coliform bacilli, enterococci or of coagulase-positive staphylococci as a response to the use of CTC. There appeared to be a selective favouring of resistant strains during storage of the treated poultry. Resistant organisms of the pseudomonas group were numerically dominant in spoiled "untreated" poultry, but were less numerous than resistant achromobacter species in the CTC treated samples.

The average count of psychrophilic yeasts in the presence of CTC was 50-fold greater than in the untreated specimens. No yeasts that would grow at 35°C. were found, and therefore it was concluded that yeasts pathogenic to man were not present in significant numbers.

Staphylococci were found in relatively small numbers and there was little increase during storage, either in the presence or absence of CTC.

Salmonellae were isolated from 14 untreated and from one treated specimen. Recovery of salmonellae in the spoiled condition was limited to two untreated carcasses; *Salm. gallinarum*, *Salm. typhi-murium*, Salm. Oranienburg and Salm. Indiana were the 4 serotypes recognized.

All strains grew in broth containing 0·21 p.p.m. CTC, but none grew at a concentration of 0·43 p.p.m.

It was concluded that CTC treatment encouraged a selective development during storage, of resistant spoilage organisms, particularly psychrophilic bacteria and yeasts.

Under refrigerated storage, there was no indication of an increased health hazard due to the presence of staphylococci, enterococci, coliform bacilli or pathogenic yeasts.

The recovery of salmonellae appeared to be reduced in the presence of CTC and salmonella-resistant to greater than 7 p.p.m. CTC was not found among the 15 cultures isolated from a total of 170 carcasses.

Betty C. Hobbs

SADLER, W. W., YAMAMOTO, R., ADLER, H. E. & STEWART, G. F. **Survey of Market Poultry for *Salmonella* Infection.** *Applied Microbiol.* Baltimore. 1961, Jan., v. 9, No. 1, 72–6. [11 refs.]

Examples were taken over a period of 20 months in 8 large processing plants in the Sacramento and San Joaquin valleys of California, and one in the San Francisco area. The plants processed fryer chickens, hens, and turkeys from all areas of northern California and turkeys from Nevada.

Every 100th carcass was sampled as it passed the official inspection point, carcasses showing evidence of disease were also sampled, and in such cases the 10th normal carcass following was also examined. The liver and a section of the intestines, including the caecum were excised. About 45 paired samples were taken on each sampling day. There were 6 mass samplings, of intestines only, made in turkeys taking every 2nd to 4th carcass; pieces of caecal tonsil and faeces were examined for salmonellae.

The media that appeared most satisfactory were selenite-cystine broth for liquid enrichment and brilliant green agar for plating.

On 21 sampling days turkeys only were processed in

the plant selected, on 14 days fryer chickens only, on 12 days chicken hens. Turkeys and fryer chickens were processed in the same plant on 1 day, turkeys and chicken hens on 1 day; and both fryer chickens and hens on 4 days.

Salmonellae were isolated from the intestinal tracts of infected birds processed on 16 (30%) of the 53 sampling days. Turkeys were positive on 10 (43%) of the 23 days they were being examined, chickens on 5 (19%) of 19 days, and hens on 2 (12%) of 17 days. A total of 94 flocks was sampled. 21 flocks (22%) were found to contain infected birds, 13 (37%) of 35 turkey flocks, 5 (18%) of 28 fryer flocks, and 3 (10%) of 31 chicken hen flocks. Salmonellae were not isolated from a liver but in two lots of fryer chickens salmonellae were isolated from the pericardial exudate as well as from the intestines, but there was evidence of gross pathological disturbances.

Salmonella typhi-murium was the type most frequently isolated from turkeys, 43 of 57 isolations, it was also found in 2 of the 3 positive flocks of chicken hens. *Salm. infantis* and Salm. bredeney predominated in the fryer chickens, and *Salm. infantis* was found in 4 of the 5 positive flocks.

It is suggested that if the size of the sampling had been raised to the range necessary for a 99% confidence level, an even greater percentage of positive sampling periods (approaching 100%) would have been found.

The isolation of salmonellae was usually associated with disease in fryer chickens but seldom in turkeys. Infected or carrier birds were being processed on 43% of the sampling days for turkeys, 26% for fryer chicken and 12% for hens.

With turkeys, salmonellae-infected birds were detected on twice as many sampling days with mass sampling as with small-sample techniques. *Betty C. Hobbs*

YAMAMOTO, R., SADLER, W. W., ADLER, H. E. & STEWART, G. F. **Comparison of Media and Methods for recovering *Salmonella typhimurium* from Turkeys.** *Applied Microbiol.* Baltimore. 1961, Jan., v. 9, No. 1, 76–80. [11 refs.]

The source of material for this study and the quantitative methods used have been described by YAMAMOTO *et al.* (*Amer. J. Vet. Research*, 1961, in the press).

Experiments with pure cultures of *Salmonella typhimurium* indicated that the highly selective media used for enumeration did not inhibit growth and that counts were comparable by the pour-plate, drop-plate, and the most-probable-number methods of enumeration; although the drop-plate technique was regarded as simple to perform and advantageous because counts could be obtained in 24 hours.

The number of salmonellae in faeces was not changed appreciably by holding the samples 24 to 48 hours at 4°C., when Ringer's solution was as effective as Hajna's preservative medium, but Hajna's medium depressed the growth of extraneous bacteria.

Faeces suspended in Ringer's solution and held for 24 hours at room temperature showed a 100- to 10,000-fold increase in numbers of salmonellae compared to control counts; this was not observed with Hajna's preservative at room temperatures.

The following media were compared: tetrathionat broth plus brilliant green, selenite broth plus cystine selenite-brilliant-green sulphapyridine broth (Osborne and Stokes), tryptose phosphate broth. The agar sub-culture media consisted of brilliant-green agar plus 0·1% sulphapyridine [OSBORNE and STOKES, this *Bulletin*, 1956, v. 31 444].

All media except the Osborne and Stokes broth were prepared from commercially dehydrated products. With some of the media, certain ingredients were added as recommended by the authors.

For the isolation of *Salm. typhi-murium* from infected tissues and other material, selenite cystine broth with subsequent plating on to brilliant green agar, gave the most favourable results. The efficiency of the various media was not governed solely by the number of organisms present in the inoculum, other factors such as the presence of extraneous bacteria, amounts of solids and type of selective ingredients, were significant factors. *Betty C. Hobbs*

ATKINSON, J. W. **Suggestions for dealing effectively with Poultry Hygiene Problems.** *Amer. J. Public Health.* 1961, May, v. 51, No. 5, 723–31. [10 refs.]

In this paper the author discusses the major problems of poultry hygiene in the United States and also the official control of these problems by the Poultry Products Inspection Act of 1957 which is being "supplemented by an increasing number of state and local programs for the sanitary supervision of processing plants in intrastate commerce and of the local distribution and sale of poultry and poultry products".

There is a good discussion of poultry hygiene programmes with a long outline list of the many items of importance to which careful attention must be given to render such programmes effective. The success of these programmes depends also on adequate co-operation between all the official agencies concerned whether local state or federal.

It is suggested that more research and field investigations on sanitation and epidemiological problems would give valuable results. Emphasis is also placed on the point that when there is conflict between the interests of public health and those of the food industry "health and consumer considerations should take precedence over purely economic and competitive interests of agriculture and industry". *M. E. Delafield*

EVELYN, T. P. T. & MCDERMOTT, L. A. **Bacteriological Studies of Fresh-Water Fish. I. Isolation of Aerobic Bacteria from Several Species of Ontario Fish.** *Canadian J. Microbiol.* Ottawa 1961, June, v. 7, No. 3, 375–82. [46 refs.]

"A total of 350 fish were taken from Ontario waters and examined for the presence of aerobic bacteria. Trout species accounted for 97·1% of the fish examined, and the remainder were 'coarse' fish. A total of 1,189 cultures of bacteria were isolated from hearts, livers, kidneys, spleens, muscles, and slime of the fish and from 11

of the waters they inhabited. Of this total, 221 cultures were lost through death, most of these organisms being too fastidious to survive the routine cultural methods employed. Of the remaining 968 cultures, 121 proved impossible to identify or group on the basis of common characteristics. The remaining bacteria were classified to the rank of genus as follows: 234 *Pseudomonas*, 140 *Aeromonas*, 111 *Micrococcus*, 96 *Lactobacillus*, 72 *Escherichia*, 57 *Brevibacterium*, 29 *Paracolobactrum*, 28 *Aerobacter*, 24 *Proteus* and other urea splitters, 18 *Alcaligenes*, 14 *Bacillus*, 11 *Achromobacter*, 7 *Streptococcus*, and 6 *Flavobacterium*."

KÖHLER, F., SCHNEIDER, W. & BECK, E. Hygienische Forderungen bei der Behandlung von Speiseeis. [**Hygienic Requirements in the Manufacture and Handling of Ice Cream Foods**] *Ztschr. f.d.g. Hyg. u. ihre Grenzgebiete.* Berlin. 1961, May, v. 7, No. 5, 355–68. [39 refs.]

In this paper there is a detailed survey of the legal provisions in relation to ice cream and similar foods which are operative in the German Democratic Republic.

In certain respects these legal requirements are inadequate and a new official memorandum has been prepared for circulation in Potsdam which is intended to be not only a basis for hygienic inspection but also to serve as a help and a model for the manufacturers.

This memorandum, here described in detail and discussed, is in sections on licensing; requirements in respect of premises, utensils and machines; raw materials and criteria of their quality; conditions of manufacture; marketing of ice cream products and the health and personal hygiene of employees. *M. E. Delafield*

DEL VECCHIO, V., D'ARCA SIMONETTI, A. & D'ARCA, S. Indagine sullo stato igienico della "crema di latte" e della "panna montata" in vendita nella città di Roma. [**An Investigation on the Hygienic Condition of Ordinary Cream and of Whipped Cream on Sale in Rome**] *Nuovi Ann. d'Igiene e Microbiol.* 1960, Nov.–Dec., v. 11, No. 6, 465–82. [24 refs.] English summary.

86 samples of cream and 86 of whipped cream taken from shops, bars, etc., between October 1958 and May 1959 were examined by a total bacterial count, *coli* count, *in vitro* examination for shigellae and salmonellae, *in vitro* and *in vivo* tests for *Myco. tuberculosis*, and *in vivo* tests for brucellae. About 90% of the samples had been supplied by one central agency, the rest by small producers. The methods of examination were those described in *Standard Methods for Examination of Dairy Products* published by the AMERICAN PUBLIC HEALTH ASSOCIATION (10th ed. New York, 1953). Whipped cream was placed in a water-bath at 25°–30°C. for 20 minutes to make it less viscous. The *coli* determination was done on the method of the most probable number, with first culture on broth containing lactose, Victoria Blue 4 R and phenol red and then subculturing on Levine's medium. Shigellae and salmonellae were sought by Difco SS medium. For brucellae, 2 ml. of cream or of whipped cream were inoculated subcutaneously in guineapigs. Animals giving positive agglutination at 1 in 10 (no higher were obtained) were killed the week after, and their organs cultured, and the remainder were killed after 8 weeks (but the organs of these were not cultured). *Myco. tuberculosis* was sought by seeding on Petragnani's medium and by subcutaneous inoculation of about 2 ml. in each of 2 guineapigs which were observed for 3 months. Samples were also tested for the presence of alkaline phosphatase, following CORNELL's procedure as in "Standard Methods".

Total counts were high both for cream and whipped cream, only in very few instances being less than 500,000 per ml. and often exceeding 50 million, with no apparent difference between the allegedly pasteurized and the non-pasteurized supplies. Not a single sample contained less than 500 coliforms per ml., most containing far more. The authors consider these findings very disturbing and note the contrast with ice-cream whose sale is forbidden if it contains more than 10 *Escherichia coli* per ml. They attribute these bad results to a general neglect of hygienic measures and probably either to inefficient pasteurization or to contamination after heat treatment. *Shigella flexneri* was isolated from 4 samples, and *Sh. sonnei* from 2. No brucellae or *Myco. tuberculosis* were detected. Ordinance No. 2972 of 1956 of the Commune of Rome lays down a limit of 200,000 total count per ml. at 37°C. and absence of *E. coli* from 0·1 ml. for cream to be used as food and orders pasteurization, but evidently these regulations are not observed.

E. Agius

ANN. INST. PASTEUR DE LILLE. 1960, v. 11, 1–231, numerous figs. [Numerous refs.] Microbiologie des eaux minérales des sodas et des jus de fruits en récipients hermétiquement clos. Le 3ème Symposium International de Microbiologie Alimentaire, Evian-les-Bains (Haute-Savoie) France, 5–9 Sept. 1960. [**Symposium on the Microbiology of Mineral Waters and Fruit Juices in Sealed Containers.**] [ASS. INTERNAT. SOC. MICROBIOL., Sect. Microbiol. et Hyg. Substances Alimentaires.]

The following categories of drinks were involved:—

(a) "*Mineral waters*", which are non-carbonated or carbonated and include the English soda water.

(b) "*Sodas*", in the French sense, which includes a great variety of waters fabricated with sugar and acid in various amounts, and sometimes containing a proportion of fruit juice or other flavourings, preservatives or other miscellaneous additions. All these drinks have in common the presence of available carbon sources in sufficient quantity to allow fermentation.

(c) *Fruit juices*, which, according to Continental definitions are natural juices with or more often without permitted preservative.

The various fruit squashes common in Britain fall between (b) and (c) but they are more like those of the (b) category, there are few natural juices of the (c) group.

These distinctions are important microbiologically. The mineral waters are treated generally like water, with a routine microbiological examination similar to that for water supplies, and the results should comply with standards for the purity of water; carbonation is

important because it is shown to have significant antimicrobial effects.

Counts of 1,000–200,000 were described for some non-gaseous mineral waters, and there might be slow but extensive development of autotrophic bacteria such as *Xanthomonas, Pseudomonas, Achromobacter* and *Flavobacterium* which could be inhibited by carbon dioxide. There are non-legal microbiological standards and it was suggested that mineral waters maintained in hermetically sealed containers should be allowed preservatives.

The microbiological flora of the sodas includes a much wider range of organisms, not only the fermenting species but also miscellaneous contaminants from the various ingredients which may be added.

The *p*H and chemical constitution, including preservative content, of drinks influenced the death rate of organisms, but these factors were constantly changing and could not be relied upon to maintain sterility; carbon dioxide under pressure was bactericidal for *Escherichia coli.* Acidity alone would not make the drinks safe and this was particularly true for low acid products such as tomato juices. *E. coli* died more quickly on storage at 37°C. than at 4° or 20°C.

The occasional mass pollution of drinks with *Pseudomonas, Saccharomyces* and *Bacillus* species was described; *Candida tropicalis,* Providencia organisms of the Paracolon group, *Staph. aureus,* and *Strep. faecalis* had been found. Pathogenic enterobacteria did not survive more than 1 day in lemon juice, in fruit juice at *p*H 3·0 more resistant types survived 35 days at 0°C. and 10 days at room temperature. Pathogens in tomato juice died during a period of 30 days.

The frequent occurrence of anaerobes in fruit juices was a noteworthy observation; *Clostridium botulinum* type A was able to multiply in acid fruit juice in some circumstances, although no toxin was found. This observation has serious implications if the mixing of fruit products with less acid materials is considered.

General matters of technique included comparative tests on the MPN and membrane filter techniques for the microbiological examination of drinks. Whole bottles of drink were used for membrane filtration which was 3–5 times as efficient as the MPN test; it was possible that inhibitory factors prevented isolation from lactose broth. The osmophilic balance of filters could be altered to study syrups.

Re-usable stoppers were regarded as undesirable because of the risk of contamination; metallic crown closures were of excellent microbiological quality. To improve the purity of drinks it was suggested that they should be filled hot into sterilized bottles. New developments for "in-place" cleaning of equipment and an experimental machine for the washing of small glass bottles was given.

Suggestions for elimination of bacteria from fruit juices included ionizing radiation and H ion exchanges. The application of combinations of preservatives in sub-lethal doses to the raw materials was said to be more effective than a single preservative such as sodium sulphite or benzoic acid used alone. The resistance of yeasts to benzoate depended on the nutrients available in the medium; in particular, less sodium benzoate was needed to inhibit yeasts if sucrose was used in place of glucose.

Recommendations for inhibiting thermo-resistant moulds in fruit juices included the use of mould-free materials and equipment, the effective washing and disinfection of factories, the application of highest possible pasteurization temperatures, the exclusion of air from bottles and the addition of ascorbic acid to preserve reducing properties. Naturally occurring ascorbic acid was important and sulphur dioxide acted as an antioxident.

Microbiological standards were proposed for mineral waters but not for fruit juices or their bottles, because normal results were impossible to define at present.

Betty C. Hobbs

FOOD POISONING

i. McFarren, E. F., Schafer, Mary L., Campbell, J. E., Lewis, K. H., Jensen, E. T. & Schantz, E. J. **Public Health Significance of Paralytic Shellfish Poison.** *Advances in Food Res.* 1960, v. 10, 135–79, 5 figs. [Numerous refs.]

ii. Banner, A. H., Scheuer, P. J., Sasaki, S., Helfrich, P. & Alender, C. B. **Observations on Ciguatera-Type Toxin in Fish.** *Ann. New York Acad. Sci.* 1960, Nov. 17, v. 90, Art. 3, 770–87, 2 figs. [24 refs.]

iii. Hessel, D. W., Halstead, B. W. & Peckham, N. H. **Marine Biotoxins. I. Ciguatera Poison: some Biological and Chemical Aspects.** *Ann. New York Acad. Sci.* 1960, Nov. 17, v. 90, Art. 3, 788–97, 4 figs. [36 refs.]

iv. Murtha, E. F. **Pharmacological Study of Poisons from Shellfish and Puffer Fish.** *Ann. New York Acad. Sci.* 1960, Nov. 17, v. 90, Art. 3, 820–36, 9 figs. [25 refs.]

v. Burke, J. M., Marchisotto, J., McLaughlin, J. J. A. & Provasoli, L. **Analysis of the Toxin produced by *Gonyaulax catenella* in Axenic Culture.** *Ann. New York Acad. Sci.* 1960, Nov. 17, v. 90, Art. 3, 837–42, 1 fig. [14 refs.]

vi. Schantz, E. J. **Biochemical Studies on Paralytic Shellfish Poisons.** *Ann. New York Acad. Sci.* 1960, Nov. 17, v. 90, Art. 3, 843–55. [37 refs.]

These papers are concerned with clinical and public health aspects of paralytic shellfish poisoning and ciguatera toxin in fish; the identification of the toxins

and the relationship of these intoxications to other fish poisons. [The word ciguatera (according to Dorland's Medical Dictionary) refers to a disease thought to be caused by eating poisonous fish.]

Together with shellfish poisoning, HALSTEAD gives five major categories of fish whose flesh may become dangerous to eat—sharks and rays; spp. of *Gymnothorax*, or moray eels; scombroid fishes; puffers, and very many species of edible fish that may cause ciguatera poisoning, (Halstead, 1959, Cambridge, Md., *Dangerous Marine Animals*, Cornell Maritime Press). To these, BANNER *et al.*, in paper 2 add "hallucinatory mullet poisoning" [HELFRICH and BANNER, this *Bulletin*, 1960, v. 35, 873] and a type tentatively called clupeoid poisoning—a seasonal intoxication of sardine-like fish, about which there have been widespread, but incomplete, reports through the islands of the tropical Pacific and Indian Oceans. These two are distinguished from ciguatera poisoning on clinical and epidemiological grounds. Most of these intoxications have similarities, but scombroid poisoning is distinct, being caused by a histamine-like toxin resulting from contamination with the bacterium *Proteus morgani* (KAWABATA *et al.*, *Bull. Japan, Soc. Sci. Fisheries*, 1956, v. 22, 41).

Ciguatera is caused by a neurotoxin occasionally found in a wide range of unrelated species of marine fishes in seas between latitudes 35° North and 34° South. It is most prevalent in the tropical Pacific and West Indies, and the disease appears to be on the increase. Characteristically its occurrence is regional, limited to definite islands or to narrow regions of those islands, and there are rapid dramatic changes in toxicity of different species of fish, from time to time, and from place to place.

Banner *et al.* (paper 2) have developed two methods of bioassay, working with toxin from the flesh of the large red snapper *Lutjanus bohar* (Forskål), one of the most consistently toxic fish in the Pacific. The mongoose *Herpestes mungo* can be used for feeding tests. It can be fed, and will retain, up to 15% of its body weight of raw fish directly, or will eat dried fish, or fish extracts mixed with raw egg. Reactions are similar to those in man and are classified: 0, no reaction; 1, slight weakness and flexion of forelimbs; 2, slight motor ataxia, more pronounced flexion of forelimbs, and weakness of hind limbs; 3, moderate motor ataxia with weakness and partial paralysis of limbs and body musculature; 4, acute motor ataxia and extreme weakness, capable of only limited movement, or coma; 5, death. All reactions are accompanied by a tarry loosely formed stool; reactions 3, 4 and 5 are sometimes accompanied by excessive salivation and trembling. Post-mortem examination showed no pathological condition other than a tendency, probably non-specific, to develop gastric ulcers. There were no morphological changes in the nervous system either after death from acute poisoning or after 1 month's feeding with sublethal doses of fish. Cats are also susceptible and react in a similar way. They are less suitable as test animals as they often regurgitate the test meal. Both animals consume too much fish for them to be ideal as test animals for quantitative bioassays. Other susceptible animals were the laboratory mouse, crayfish and turtle, all of which presented difficulties with feeding.

The same authors describe in detail the preparation of an alcoholic and ethereal extract of the flesh of toxic fish for intraperitoneal injection into mice, which they have developed successfully. This promises to become a practical qualitative method of bioassay. A table illustrates an evaluation of the method for extracts from different samples of fish whose toxicities were determined by the mongoose feeding test as highly toxic, moderately toxic and non-toxic, at dosages from 0·1 to 1·5 mgm./gm. giving the mean time of death in minutes of 2 mice tested at each level of dosage. There is a good correlation between the two tests.

Comparison of these methods with tests based on the injection of water-extracts of flesh (HALSTEAD and BUNKER, *Zoologica*, 1954, v. 39, 61) showed that this earlier test is unreliable. The solubility of the toxin differs considerably from the paralytic toxin of shellfish, described below, in that it is not readily extracted with water or methanol, and is highly soluble in ethanol diethyl ether, acetone and chloroform.

Incidental to the main investigation of *L. bohar* 15 other species of fish were found to be toxic when tested by mongoose feeding, producing identical reactions. Among these were specimens of *Gymnothorax javanicus*, and it may be that moray-eel toxin is the same as that in ciguatera.

Hessel *et al.* (paper 3) found that ciguatera toxin, obtained in an acetone and ether-soluble extract of fish muscle, has an inhibitory effect on the action-potential of excised frog sciatic nerve. Measurement of reduction of the action-potential generated by maximal stimulation of an excised nerve preparation bathed in toxic emulsion has been developed as a test. Using this assay to study the frequency of toxicity and concentration of poison in *L. bohar*, they have shown that increasing fish-size is paralleled by an increase in both percentage of toxic fish and concentration of poison in the fish.

The source of ciguatera toxin and its chemical structure are still unknown, but stomach-content, toxicological, and algological analyses have suggested that species of blue-green algae, particularly of the genus *Lyngbya* may be responsible. Banner *et al.* (paper 2) examined *L. majuscula* which caused outbreaks of "swimmer's itch" at Hawaii, but considered that this dermatitis toxin was not identical with ciguatera toxin from *L. bohar*. They have isolated a non-crystalline substance from their alcohol and ether extract of *L. bohar* which is lethal to mice in 14 minutes on injection at 65 μgm. per gm.

McFarren *et al.* (paper 1) review the literature concerning paralytic shellfish poisoning, and give an account of recent research into the assay of the shellfish toxin. Their review covers: related naturally occurring poisons; source of the poison; dinoflagellates involved and their ecology; ecology and distribution of toxic shellfish; physiology and toxicology of the poison; isolation and characterization of the poison; stability and detoxification of the poison; prevention and control of shellfish poisoning; research needs.

Shellfish poisoning is associated with the appearance of "blooms" or "red tides" caused by dense populations of plankton. Along the Pacific coast of North America, for several years, the source of the poison has been considered on epidemiological and ecological grounds to be the dinoflagellate *Gonyaulax catenella*. On the Atlantic coast in the Bay of Fundy, *Gonyaulax tamarensis*, and in Belgium (where poisonous mussels were

obtained from brackish estuarine waters) a dinoflaggelate described as *Pyrodinium phoneus*, have been suspected. Various types of plankton feeder may become poisonous, but the principal shellfish concerned are mussels and clams. There was one report (in 1957 in British Columbia) of oyster poisoning, and the poison has been detected in both Pacific and Atlantic oysters. Scallops become toxic, but usually only the non-toxic adductor muscles are eaten. Ingested poison tends to accumulate in the digestive gland of mussels and clams, the gills of the soft shell clam, and the siphons of butter clams; mussels tend to eliminate the poison rapidly, but butter clams retain it in their siphons for a long time. Over 40 incidents of paralytic shellfish poisoning are recorded, from the death in 1793 of one of Captain Vancouver's seamen on Vancouver Island, to outbreaks in 1957. These involved some 790 known cases and 170 deaths, distributed over the Atlantic and Pacific coasts of U.S.A. and Canada, the northern Atlantic coasts of Europe, South Africa, and New Zealand. Species of shellfish that have been incriminated are: mussels—*Mytilus californianus* [see SOMMER and MEYER, this *Bulletin*, 1938, v. 13, 226], *M. edulis* (black mussel) and *Donax serra* (white mussel); clams—*Saxidomus nuttallii* (Washington clam), *Saxidomus giganteus* (butter clam), *Siliqua patula* (razor clam), *Mya arenaria* (soft shell clam), *Spisula solidissima* (bar clam); oysters—*Crassostrea gigas* (cultivated Pacific oysters); scallops; sand crabs. The public health risk has varied considerably in different species in different outbreaks; the black mussel caused no cases in San Francisco, but was poisonous on the Atlantic coast and in South Africa. Razor clams were rarely toxic in British Columbia, but were comparable to mussels at San Francisco.

The isolation and investigation of chemical and physical properties of the poison and methods of assay are described in detail both in paper 1 and by Schantz in paper 6, to which further reference is made below. Clam and mussel poisons are white solids, formula $C_{10}H_{17}O_4N_7 \cdot 2HCl$, hygroscopic, extremely water soluble, soluble in methanol and to some extent in ethanol, and insoluble in the usual lipid solvents. They give a colour reaction with certain aromatic nitro compounds in alkaline solution—Behre and Jaffe reagents—(in much the same way as creatinine), and this reaction is not given if oxidation or reduction destroys toxicity. A modification of the Jaffe colour test for the chemical assay of the poison has been developed and this has proved more accurate than bioassay in the laboratory, but is not yet suitable for field work.

A mouse bioassay is based on a mouse-unit, originally defined as the minimum amount of poison to kill a 20 gm. mouse in 15 minutes on the intraperitoneal injection of 1 ml. of aqueous extract prepared to standard specifications. Variability of mouse-units because of different susceptibilities of mouse strains, and other factors, have been overcome by the use of a reference-standard containing a known amount of the purified poison. From this a conversion factor (or CF value) to convert mouse-units to μgm. is obtained. The average CF value is of the order of 0·191 μgm. per mouse-unit. This standardized mouse-assay is now the official method of the Association of Official Agricultural Chemists, and samples of pure poison for standardization are available from the U.S. Public Health Service.

Previously accepted limits for toxin were 400 mouse-units per 100 gm. of shellfish (=80 μgm. per 100 gm.). Cooking tends to destroy toxin, though, because of solubility, cooking waters may become extremely toxic. In canning much of the bouillon is discarded, so that a great deal of toxin is lost. Accepted limits for cans are 200 mouse-units for 100 gm. of contents of the can, and because of the destruction of toxin such a product may be obtained from raw shellfish containing 1,000 mouse-units per 100 gm. Shellfish can become poisonous in affected areas very rapidly, 100-fold increases can occur in a few days, and there is a record for soft clams of an increase of from 542 mouse-units to 26,180 mouse-units per 100 gm. within 6 days.

The lethal dose for man is influenced by considerable variations in tolerance. Recent investigations have recorded deaths after ingestion of 5,800 mouse-units (1,102 μgm.), 2,400 units (456 μgm.); a child suffered serious poisoning from 600 units (96 μgm.); mild to severe symptoms have occurred after 650 units (124 μgm.) to 2,150 units (344 μgm); and there has been recovery after very severe illness after ingestion of 5,550 units (880 μgm). Symptoms of poisoning in man start with tingling and numbness about the lips and mouth 5–30 minutes after ingestion, followed by numbness or pricking in finger tips and toes within 4–6 hours, progressing to arms, legs and neck with peripheral paralysis of voluntary movements, accompanied by subjective symptoms of lightness. Reflexes are normal, mentality is clear, pulse 80–100, temperature slightly sub-normal (mean 98°F.). There are no significant post-mortem findings.

Murtha (paper 4) has made a comparative study of purified mussel and clam poisons, and the crystalline hydrochloride of puffer poison. The pharmacology of mussel and clam poisons, like their chemical structure, appears to be identical; cardiovascular collapse with a rapid fall in blood pressue is due in part to central effects on the brain, and in part to direct effects on the myocardium; the poisons are powerful neurotoxins producing complete depression of both peripheral nerve and reflex transmission. Puffer poison has different pharmacological effects. It is less toxic to the dog and cat, has slight or negligible cardiotoxic effects on the myocardium, but causes a marked fall of blood pressure and respiratory failure, apparently by direct action on respiratory and vasomotor centres; there is neuromuscular paralysis associated with an ascending type of paralysis.

Burke *et al.* (paper 5) were able to obtain toxin from pure cultures of *Gonyaulax catenella* and have demonstrated that it is identical with mussel toxin. This indicates that California mussels and butter clams obtain their toxin from *G. catenella.*

Schantz (paper 6), reporting on the chemistry and isolation of toxin from California mussels *Mytilus californianus* and Alaska butter clams *Saxidomus giganteus* and scallops *Pecten grandis*, concludes that some of the chemical qualities of scallop poison are different from those of clam and mussel poisons. The poisons are derived from toxic plankton; they are among the most potent known to man; their mode of action remains unexplained.

The prevention and control of shellfish poisoning has been handicapped by the absence of reliable techniques to predict the occurrence of toxic shellfish, and of specific prophylactic or therapeutic measures. Prevention depends principally on field sampling laboratory testing, and public education programmes, supported by appropriate legislation. In affected areas, notably the Pacific and North Atlantic coasts of North America, in the absence of information concerning toxicity or the prevalence of toxigenic plankton, the viscera of mussels, the siphons of clams and the raw meat of any shellfish should not be eaten, and the cooking waters should not be drunk.

T. P. Eddy

BAKER, T. D. & HAFNER, W. G. **Cadmium Poisoning from a Refrigerator Shelf used as an Improvised Barbecue Grill.** *Pub. Health Rep.* Wash. 1961, June, v. 76, No. 6, 543–4. [10 refs.]

This is an interesting short account of a family outbreak of poisoning in which symptoms of headache, severe nausea and vomiting occurred within 1 hour of eating an evening meal prepared out of doors. All 4 members of the family—2 adults and 2 children—were affected. By midnight the symptoms began to subside and no ill-effects were noted next day.

None of the food which had consisted of steak, potatoes and green vegetables was available for examination. On enquiry it was learnt that the steak was grilled on an improvised outdoor barbecue consisting of an old refrigerator shelf which was being used as a grill for the first time.

This shelf was examined chemically and the plating remaining on it was found to contain cadmium in greater than trace amounts. It is believed that under the conditions of heating such a worn metal shelf cadmium would get into the steak in sufficient amount to cause illness, for as little as 10 mgm. of cadmium has been reported to cause symptoms of poisoning.

There is some discussion with reference to the literature on cadmium poisoning in which it is stated "Cadmium ingestion rarely leads to death, while cadmium inhalation often does". The symptoms of the 2 forms of poisoning are so different that the 2 conditions could not easily be confused. *M. E. Delafield*

BALDOVIN-AGAPI, Coralia, MIHALCO, Florica, BORŞAI, Leia, CHIRESCO, Margareta, PANAITESCO, G. E., GRIGORIU, T. & MUNTEANU, Natalia. Considérations sur les épidémies streptococciques d'origine alimentaire. **[Considerations on Food-Borne Streptococcal Epidemics]** *Arch. Roumaines Path. Expér. et Microbiol.* 1961, June, v. 20, No. 2, 191–200. [19 refs.]

The English summary appended to the paper is as follows:—

"An epidemic of food-borne streptococcal angina is described. It was caused by streptococci of A group, type 11/27, and involved 42·00% of a total of 207 subjects aged 30–35 years, who were taking their meals in the same canteen.

"Bacteriological investigations demonstrated the existence of 3 cases of angina and of 3 healthy carriers harbouring the same type of streptococcus among the staff of the canteen. These subjects are considered to have contracted the infection during the epidemic. The source of the infection probably was a female member of the staff, who was suffering from chronic sinusitis. However, the presence of the streptococcus could not be demonstrated in this case since the patient was examined after undergoing penicillin treatment.

"The epidemic described is the second in chronologicol order of four food-borne epidemics caused by this type of streptococcus in Roumania during the period 1956–1959.

"The paper contains comments on food-borne epidemics caused by pyogenic streptococci in various countries during recent years. It is pointed out that although the epidemiological mechanism in such cases is similar to that in food poisoning, these epidemics differ from the later by a period of incubation and a clinical symptomatology characteristic of air-borne streptococcal infections in which digestive disorders play a minor part or are altogether absent."

NOUR EL-DIN MUSTAFA, M. **The Mode of Contamination of Food Articles in Food Poisoning Outbreaks. A Critical Review with Report of Two Outbreaks.** *J. Egyptian Med. Ass.* 1960, v. 43, No. 11, 861–74. [26 refs.]

A review is given with examples of chemical food poisoning including arsenic, antimony, lead, copper, tin, food perservatives and insecticides, and also bacterial food poisoning from salmonellae, staphylococci, other organisms and also botulism. 2 outbreaks are reported.

One followed the consumption of a contaminated sour drink known as Sobia, and the second was due to a poison present in bread made by a bakery in Cairo. Sobia is made from polished rice boiled in water for several hours to form a thick homogeneous paste which is then cooled and sieved with the help of vigorous rubbing by hand; a souring agent including a portion of the sour drink prepared the previous day containing lactic acid bacilli, yeast cells, *Streptococcus lactis* and haemolytic anthrocoids is added to the fine paste. The mixture is fermented overnight in a warm room and is again strained with vigorous rubbing by hand. Sugar, milk, cinnamon and ice are added immediately before consumption. 300 persons, followed 2 weeks later by another 19, were taken ill from 2 to 4 hours after consumption of the drink, with nausea, vomiting, colic, sweating, rapid weak pulse and diarrhoea. Stomach lavage followed by magnesium sulphate solution was carried out and stimulants such as chloramine and camphor were injected. Patients recovered after 2 days and there were no fatalities. Coagulase-positive staphylococci isolated in large numbers from unfermented samples of the drink and from the hands of 2 workmen preparing the drink, one of whom showed partially healed septic wounds on his fingers, were serologically identical. Streptococci isolated also from the drink and the workers' hands showed a similar sensitivity to penicillin. No staphylococci were isolated from the fermented drink samples as the souring organisms inhibited

their growth. It was thought that the addition of the souring agent to the rice paste had been delayed for a time sufficient to allow toxin production in the paste.

In the second outbreak 257 persons, mostly children, were taken ill half to 1½ hours after consumption of sandwiches. Symptoms included nausea, vomiting, severe colic without diarrhoea, flushing, headache, respiratory difficulty, cyanosis of lips and nails, tremors, convulsions, contracted pupils, slow pulse, high blood pressure, pulmonary oedema and subnormal temperature. 67 patients recovered on the same day, 161 after 2 days, and 29 died, the majority within 4 to 14 hours after admission to hospital and mostly children 2 to 12 years old. Post-mortem findings revealed ulceration and haemorrhagic spots in the stomach, congestion of the intestines and oedema of the lungs. Chemical analysis revealed the presence of the organic phosphate insecticide parathion in bread used for the sandwiches and in the dough used in the bakery preparing the bread. It seemed that the parathion used extensively as an insecticide had accidentally contaminated the bread during its preparation.

Betty C. Hobbs

See also p. 1035, DRYL *et al.* [**A Milk-Borne Epidemic of Typhoid Fever in Zgierz and Lodz in 1950**].

WHITEHEAD, E. N. **Investigation of an Outbreak of Food Poisoning due to *Salmonella typhi-murium*.** *Sanitarian.* London. 1961, Apr., v. 69, No. 7, 321–3.

58 of 900 people including children were infected by raw TT [tuberculin tested] milk contaminated with *Salmonella typhi-murium* during October and November 1960. The dairy, run by the owner and one employee, sold 50 to 60 gallons per day of raw TT milk bottled on the premises but purchased from a farm nearby. The dairyman and his family lived on the premises, the employee elsewhere. Near the house the dairyman kept several hundred hens in deep litter houses.

The farmer concerned milked about 40 cattle. One cow was clinically suspect, another had been sold to the knackers' yard, and the farmer had suffered from diarrhoea a fortnight earlier. *Salm. typhi-murium* was isolated from a milk sample taken from the dairy, from stools from 3 of the dairyman's family and his employee, from 3 members of the farmer's family and from 2 rectal swabs taken from the cattle, 1 from the sick beast. All the strains of *typhi-murium* were of the same phage type. The milk samples from the farm were negative as was the water. It was assumed that contamination must have gained access to the milk in the cowshed, the milk room or in the bottling plant of the dairy. Cowshed dung could have been responsible, and in the milk room contamination could have been introduced by vessels or by hands contaminated by the cows. At the dairy milk could have been infected in the bottling plant by the dairyman's assistant whose stools were positive, but it was suspected that the infection originated from the farm, possibly from the farmer himself. Wet weather may have helped to spread infection because the tails, legs and udders of the cattle were dirty. Other possible sources of infection were hens and grazing land.

Formal notice was served requiring heat-treatment of the milk and it is stressed that no milk is safe unless pasteurized.

Betty C. Hobbs

Mycoses and Mycology

The order of diseases and fungi in this section is:—**General; Dermatophytes; Blastomyces; Histoplasma, Sporotrichum, Phialophora; Candida, Cryptococcus; Actinomyces, Nocardia; Aspergillus; Others.**

Papers on Blastomycosis (South American type), Coccidioidomycosis, Mycetoma and Rhinosporidiosis are abstracted in the TROPICAL DISEASES BULLETIN.

BARKER, S. A. & TROTTER, M. D. **Isolation of Purified Trichophytin.** [Correspondence.] *Nature.* 1960, Oct. 15, v. 188, 232–3. [10 refs.]

In order to obviate the development of skin reactions due to impurities contained in commercial trichophytin the authors undertook its purification, using an ethylene glycol extract (crude trichophytin) of an acetone-dried preparation of *Trichophyton mentagrophytes.*

This crude trichophytin was then purified by "precipitation as a borate 'Cetavlon' complex", the various stages of this procedure being described. The Cetavlon was removed with great care by a passage down a column of Zeocarb 225 (H+) since it was found that "at a concentration of 0·1 mgm./ml., its complex with trichophytin produced violent skin reactions".

Various analytical data are also given, including those obtained by ultracentrifugal analysis which showed that trichophytin has a relatively low molecular weight, *viz.* 20,000–30,000; chromatographic analysis which showed that it contains glucose, mannose and a number of amino-acids; and ultraviolet absorption spectra which showed "a shallow peak at 270–280 mμ corresponding approximately to a 10% peptide content". The nitrogen content, as estimated by Kjeldahl, was 1·05%; finally, nucleic acid was absent from the purified product.

C. J. La Touche

MORGAN, H. G. Tratamento das tinhas com griseofulvin a por via oral. **[Treatment of Tinea with Oral Griseofulvin]** *Brasil-Médico.* 1960, June–Aug., v. 74, Nos. 23/35, 256–7.

The author, in Los Angeles, treated 26 patients with griseofulvin. 14 had lesions of the glabrous skin due to *Trichophyton rubrum* or *T. mentogrophytes* and 9 had infections of the nails due to *T. rubrum.* 2 others had pityriasis versicolor caused by *Microsporum* [*Malassezia*] *furfur* and the last had intertrigo due to *Candida albicans.*

The usual daily dosage was one 250 mgm. tablet thrice daily, although 2 to 4 tablets were given sometimes. The period of treatment varied from one week to several months. All the patients with tinea of the glabrous skin were improved (10 of them were cured) within 1 to 3 months: there were no failures. 6 of the 9 patients with nail affections were improved in 4 months, but most of those in this group are still under treatment. One of the patients with tinea versicolor was improved in 7 weeks. The *C. albicans* infection was not improved.

H. J. O'D. Burke-Gaffney

FISCHER, J. B. **Onychomycosis caused by *Scopulariopsis brevicaulis.*** *Canadian Med. Ass. J.* 1960, Dec. 10, v. 83, No. 24, 1264–5, 4 figs.

3 cases of infection of the toe-nails due to *Scopulariopsis brevicaulis* are described in this article. In all cases the structures characteristic of this fungus were demonstrated microscopically and positive cultures were obtained.

The first patient was a man aged 33 years. At examination in January 1959, he gave a history of progressive colour change and thickening in the left great toe nail, commencing "at the lateral borders and progressed to involve one-third to one-half of the nail plate".

By April 1960 the infection had spread to other nails on the same foot and to the great toe nail on the other foot.

The second patient was a man aged 36 years. The left great toe nail had become progressively discoloured and thickened over a period of 1½ years, and at examination two-thirds of the nail had become involved.

The third patient was a man aged 33 years. The inner border of his left large toe nail had become thickened and opaque and was crumbling. While no data are available concerning the treatment of the first 2 cases, this report states that griseofulvin was administered to this last-mentioned patient, without, however, any benefit.

C. J. La Touche

COZAD, G. C. & LARSH, H. W. **A Capillary Tube Agglutination Test for Histoplasmosis.** *J. Immunology.* 1960, Oct., v. 85, No. 4, 387–90, 1 fig.

An agglutination technique is described, in which capillary tubes are filled with stained particles of disintegrated yeast phase cells of *Histoplasma capsulatum* for use as antigen.

Capillary tubes 7 cm. long with an inside diameter of 0·5–0·9 mm. were filled to one-third capacity with stained antigen particles and then an equal amount of the serum to be tested was introduced into them by capillary attraction. The tubes were then placed upright in plasticine at room temperature with the antigen at the lower end. Tests were read after 1 hour. "Blue-black macroscopic clumps along the capillary column indicate a positive reaction."

Sera from 150 rabbits experimentally infected with *H. capsulatum* were tested in this manner. High titres were obtained during the active stage of the disease, but fell as it subsided, unlike complement-fixing titres, which persisted.

This technique offers, among others, the advantage that large numbers of sera can be screened in a short time, with a minimum of antigen and serum and, in addition, the reading of the end point is facilitated by the use of stained antigen.

It is hoped that it will be possible to use this agglutination technique for the purpose of testing sera from human patients, and that it will provide a simple and rapid means of diagnosis.

C. J. La Touche

LITTLE, J. A. **Benign Primary Pulmonary Histoplasmosis: a Common Cause of Unexplained Fever in Children.** *Southern Med. J.* 1960, Oct., v. 53, No. 10, 1238–40, 2 figs.

This article contains descriptions of the clinical features of 4 cases of benign primary pulmonary histoplasmosis. The patients concerned were all male children between the ages of 2¾ and 8 years inclusive. The main clinical symptom was a low-grade persistant fever. Clinical signs included adenopathy, lung infiltration and a palpable spleen; and in one patient the liver was palpable about 1 cm. below the right costal margin. The histoplasmin skin test was positive in all the patients.

After varying periods in hospital, all the patients recovered spontaneously, and this recovery was accompanied by a regression of the pulmonary lesions revealed by X-ray examination.

C. J. La Touche

HILL, G. A. & MARCUS, S. **Study of Cellular Mechanisms in Resistance to Systemic *Histoplasma capsulatum* Infection.** *J. Immunology.* 1960, July, v. 85, No. 1, 6–13, 4 figs. [13 refs.]

The purpose of the investigation described in this article was to ascertain the effect of phagocytes derived from immunized and non-immunized animals on yeast-phase cells of the *Histoplasma capsulatum in vitro* and *in vivo.*

Peritoneal exudates were prepared by injecting 1 ml. of a solution of 0·01 mgm. glycogen in saline into the peritoneal cavity of normal and immunized adult albino mice. When washed they were used for the study of their phagocytic action on the yeast-phase cells of *H. capsulatum.*

By a special technique whereby the phagocytes were allowed to become attached to coverslips it was possible to compare microscopically, after fixing the phagocyte

deposit in methanol and staining it by the periodic-acid-Schiff technique, the effect of phagocytosis in its successive stages in phagocytes derived from both immunized and non-immunized animals.

In the case of the phagocytes obtained from non-immunized animals the ingested yeast cells appeared typical and the cytoplasm of the phagocytes stained a green colour with counterstain, whereas, in the case of the phagocytes from the immunized animals the yeast cells were in various stages of disruption and the cytoplasm of the phagocytes was strongly Schiff-positive, suggesting the presence in it of material derived from the ingested yeast-phase cells.

H. capsulatum yeast-phase cells labelled with ^{32}P showed that, at first, the activity of the phagocytes from both immunized and non-immunized animals was approximately similar, but that, after the first few hours, this activity differed; thus, macrophages from immunized animals were able to limit the growth of the parasites *in vitro* for a significantly longer period and to destroy these organisms at a more rapid rate than could normal macrophages. *C. J. La Touche*

MACKENZIE, D. W. R. **Yeasts from Human Sources.** *Sabouraudia.* Edinburgh. 1961, Jan., v. 1, Pt. 1, 8–15. [46 refs.]

This article reports the results of an investigation of the yeasts and yeast-like flora of specimens obtained from various sites in the human body as well as from throat and vaginal swabs. These included the following types and numbers of specimens: urine, 182; sputum, 174; stool, 103; throat swabs, 79; vaginal swabs, 150; wounds and other lesions, 203; miscellaneous specimens, 113.

23 species were isolated, including those belonging to the group of true yeasts, such as *Saccharomyces, Hansenula* and *Pichia,* and to such genera of the yeast-like fungi as *Cryptococcus, Candida, Rhodotorula, Torulopsis, Trichosporon* and *Taphrina.*

C. albicans was the species most frequently isolated, accounting for 56% of the total number of isolates; next in order came *Torulopsis glabrata* (12·4%); and then *Rhodotorula mucilaginosa* (6·1%) and *C. tropicalis* (4·8%).

Some species were obtained more frequently from one site than from others; for example, *T. glabrata,* of which 15 out of a total of 31 isolated were from sputum; and it was the most common isolate from urine. Also, *C. albicans* was the yeast species most commonly isolated from sputum (70 isolates or 57% of total yeasts from this source) while somewhat less than half this number was obtained from both stools and throat swabs.

Special attention is given to the finding of *T. glabrata,* and its role as a pathogen is discussed.

[To those who are engaged in the study of medical and veterinary mycology this new journal is the fulfilment of a long-felt want: a new channel to receive and bear witness to the ever increasing tide of mycological information flowing in from medical and veterinary centres.

Almost all of the clinical reports of mycoses are scattered among innumerable medical journals throughout the world, many of which, owing to the language in which they are written or to international difficulties connected with obtaining them, are, notwithstanding the existence of many useful abstracting journals, virtually inaccessible to many who might benefit from being acquainted with them. This journal is the official organ of the International Society for Human and Animal Mycology. It caters for articles in 5 languages, English, French, German, Spanish and Portuguese. The editorial board is composed of prominent exponents of the subject whose international reputation is well established and whose fundamental and inspiring contributions have been largely responsible for the great progress and rapid spread of knowledge of medical and veterinary mycology in recent years. They are to be congratulated on the high standard of presentation shown in the first issue of this journal, of which some abstracts appear in these pages.] *C. J. La Touche*

RIDLEY, M. F. **A Comparison of Methods for Identification of *Candida albicans*.** Reprinted from *Australian J. Dermat.* 1960, Dec., v. 5, No. 4, 209–13, 2 figs. on pl.

The usual methods of identifying *Candida* spp. by sugar fermentation and assimilation are reliable but require pure cultures and are time-consuming. 17[illegible] isolates of *Candida* spp. were taken and identified by the methods of MARTIN *et al.* (*J. Bacteriology,* 1937, v. 34, 99) and proved to be *C. albicans* (149), *C. tropicalis* (14), *C. stellatoidea* (5), *C. parakrusei* (5), *C. krusei* (4) and *C. guilliermondii* (1). All these strains were subjected to a variety of other identification procedures as follows:—

1. *Chlamydospore production.* The media used were corn meal agar, corn meal agar plus Tween 80 and rice flour agar plus Tween 80. *C. albicans* was the only species to produce chlamydospores but not all did so; of the 149 strains of *C. albicans,* 140 produced them on rice flour agar plus Tween 80, 111 on corn meal agar plus Tween 80 and only 62 on plain corn meal agar. Production of chlamydospores was most rapid on rice-flour agar plus Tween 80.

2. *Production of "Spidery" Colonies.* The *Candida* spp. were inoculated on peptone agar and incubated at 37°C. Only 96 of the *C. albicans* produced definite "spidery" colonies and 4 other species gave a doubtful result.

3. *Germ Tube Production.* Serum was inoculated with the *Candida* spp. and incubated at 37°C. for 90 minutes; incubation was continued to 3–5 hours if the first examination was negative. All 149 strains of *C. albicans* produced germ tubes in under 5 hours, the most rapid being freshly isolated colonies, but no other species did.

4. *Reduction of Tetrazolium Compounds.* On PAGANO-LEVIN medium (*Antibiotics Ann.,* 1957–58, 137) the 149 strains of *C. albicans* varied from cream to pale pink in colour; the 4 strains of *C. krusei* were white but differed in having irregular colonies; all the other species were deep pink or red.

[The only comment necessary on this useful comparison of methods is that *C. utilis, C. rugosa* and *C. stellatoidea* can produce germ tubes in serum (Personal Communication: D. W. R. MACKENZIE, Institute of Pathology, Belfast) though these species are readily distinguishable from *C. albicans.*] *Ian G. Murray*

HASENCLEVER, H. F. & MITCHELL, W. O. **Pathogenicity of *C. albicans* and *C. tropicalis*.** *Sabouraudia.* Edinburgh. 1961, Jan., v. 1, Pt. 1, 16–21, 10 figs. (5 on 2 pls.)

This article, which is well supported by tables and graphs, contains the results of inoculation experiments with mice and rabbits designed to provide information as to the relative pathogenicity of *Candida albicans* and *C. tropicalis* for these animals.

It was found that whereas *C. tropicalis* showed a considerable pathogenicity for mice, it showed little or no pathogenicity for rabbits. *C. albicans* was generally more virulent for mice than *C. tropicalis*, but some strains of *C. tropicalis* were more virulent than some strains of *C. albicans*.

Various dilutions of yeast suspensions were injected intravenously and the LD50 for these dilutions was calculated and tabulated.

The multiplication rates of strains of these 2 species of *Candida in vivo* were also recorded for various organs. Results, which are represented as graphs, show the interesting feature that the multiplication rate of 3 strains of *C. tropicalis* in the brain rises steeply and reaches its climax at 2–4 days, and then falls off gradually, whereas in the case of *C. albicans* the rate of multiplication in the brain rises only slightly during the first few days and then falls very gradually. *C. J. La Touche*

GRESHAM, G. A. & WHITTLE, C. H. **Studies of the Invasive, Mycelial Form of *Candida albicans*.** *Sabouraudia.* Edinburgh. 1961, Jan., v. 1, Pt. 1, 30–33, 6 figs. on pl.

The effects of isoniazid on *Candida albicans in vitro* and *in vivo* are described in this article.

It was found that 0·1% isoniazid inhibited the growth of *C. albicans* in potato water. Rabbits were inoculated intravenously with 1 ml. of a suspension of *C. albicans* in saline (500 million per ml.), and divided into 4 groups of 6. Isoniazid was given to 3 groups as follows: (B) 10 mgm. intravenously at the time of inoculation; (C) 10 mgm. intravenously at the time of inoculation followed by daily doses of 10 mgm. intraperitoneally; (D) 10 mgm. intraperitoneally on the day before inoculation followed by daily doses of 10 mgm. for 7 days. No isoniazid was given to the fourth group (A) which served as control.

Results from these animal experiments showed that the rabbits in groups A and B died in 3 days; that there was no noticeable difference in the behaviour of the rabbits in these two groups, and that, while the rabbits in group C also died in 3 days, their kidneys differed markedly from those in the control group. Thus, in the control group the kidneys were "greatly swollen and oedematous with many large white lesions", whereas in group C they were smaller and the lesions also were "smaller in size and fewer in number". In group D the rabbits remained apparently well, but at autopsy at 18 days after inoculation showed inflammatory changes in the kidneys.

Histological examination of the kidneys revealed abundant mycelium in group A; blastospores and short hyphae predominating in groups B and C; and only a few blastospores and short hyphae in group D. In addition the presence of ribonucleic acid was demonstrated at the hyphal septa as well as at the hyphal tips, indicating, according to the authors, a functional continuity which "could be advantageous in colonisation of tissue remote from the point of fungal entry into the tissues". *C. J. La Touche*

KUPFERBERG, A. B. & DOSCHER, G. E. **The Antifungal Activity of 3-Trichloromethylthio-5-(1-Ethylamyl)-Hydantoin (Chlordantoin).** *Antibiotics & Chemotherapy.* New York. 1961, Feb., v. 11, No. 2, 73–8.

This paper is concerned with a series of trichlormethylthio compounds, one of which, known as Captan, has been shown to have anti-fungal activity. 12 such compounds were tested for capacity to inhibit the growth of *Candida albicans*: the most active (minimum inhibitory concentrations at *p*H 4·5 and 7·0 were 2 and 3 μgm. per ml.) was 3-trichlormethylthio-5-(1-ethylamyl)-hydantoin, to which the name Chlordantoin is given. Particulars are given of its activity against 10 other species of fungi and 6 of bacteria: most of the latter were more resistant. Activity was reduced to one-fifth by 10% serum or 1% yeast extract, but not by human vaginal fluid, and was potentiated by quaternary ammonium compounds (all in tests with *C. albicans*). Various tests showed a low degree of toxicity, and "oral, vaginal and dermal tolerance tests" gave satisfactory results. *L. P. Garrod*

KREGER-VAN RIJ, N. J. W. **Taxonomy of *Cryptococcus neoformans* and its Variety *uniguttulatus*.** *Antonie van Leeuwenhoek: J. Microbiol. & Serol.* 1961, v. 27, No. 1, 59–64.

"A comparative study of a number of strains of the species *Cr. neoformans* and its variety *uniguttulatus* showed that capsule formation was inappropriate as a character to differentiate species and variety. The ability to grow at 37°C. and to use dulcitol and *D*-arabinose as source of carbon appeared to be more suitable. A definition of species and variety on this basis was given."

DURANT, J. R., EPIFANO, L. D. & EYER, S. W. **Pulmonary Cryptococcosis: Treatment with Amphotericin B.** *Ann. Intern. Med.* 1960, Sept., v. 53, No. 3, 534–47, 6 figs. [31 refs.]

The beneficial results of intravenously administered amphotericin B in the management of systemic fungal diseases are once more demonstrated in 2 of the 3 cases of pulmonary cryptococcosis described in this detailed report.

The first case described was of a white male aged 52 years who, on admission, complained of dyspnoea, loss of weight, and a chronic cough which had started 3 weeks previously. X-ray examination of the lungs revealed what appeared to be a left upper lobe pneumonia. When, however, *Cryptococcus neoformans* was grown from the

sputum amphotericin B was administered intravenously "in increasing increments of 10 mg. daily until a total dose of 1 mg. per kilogram of body weight was obtained". The vehicle of administration was 5% dextrose in water in a dilution of 1 mgm. of amphotericin B to 10 cc. of diluent. The maintenance dose was 75 mgm. in 1,000 cc. glucose and water on alternate days for 7 weeks. Side reactions included: chills, fever, nausea, occasional vomiting, localized phlebitis and cellulitis. Discontinuation of therapy resulted in the reappearance of the organism. Thrombophlebitis was ultimately avoided by the administration of 1 cc. of 1% procaine directly into the intravenous tubing every hour. As a result the lung fields became clear after further treatment with amphotericin B.

The second case was of a male Negro aged 29 years who, besides presenting with cough, also had severe frontal headache. X-ray examination of the lungs revealed a circumscribed lesion in the right lower lobe. There was minimal nuchal rigidity and the cerebrospinal fluid [CSF] was clear; but later an India ink preparation of the CSF showed cells suggestive of *C. neoformans*. The presence of this organism was later confirmed by culture.

Chemotherapy initially included large doses of aqueous penicillin, streptomycin, salicylates and opiates. In due course a number of other drugs were administered, including finally, Actidione intravenously, in the dosage of 120 mgm. daily. However, apart from a short-lived response to this drug, the patient's condition gradually deteriorated and he died on his 59th day in hospital.

At autopsy various brain lesions were found as well as cryptococcal pneumonitis.

The third subject was a white male aged 46 years who was admitted because of haemoptysis. X-ray examination revealed a pleural effusion at the right lung base and an infiltrate in the 2nd right anterior interspace.

Initial therapy consisted of streptomycin and penicillin, but when *Cryptococcus* was found amphotericin B was administered up to a total of 2,875 mgm. over a period of 9 weeks in a dosage of 1 mgm. per kgm. in 1,000 cc. of 5% glucose and water on alternate days until the 7th week. At this time the patient developed azotaemia and consequently it became necessary to reduce the dosage to 0·75 mgm. per kgm. However, 2 weeks later X-ray examination showed clearing of the right base and the patient was discharged.

This article concludes with a discussion on the epidemiology, clinical features, pathology, mycology and treatment of this disease. *C. J. La Touche*

BEDRYNSKA-DOBEK, M. Détermination des caractères morphologiques, culturaux et biochimiques, du pouvoir pathogène et de la résistance aux antibiotiques de 9 souches de *Nocardia asteroides*. **[The Morphological, Cultural and Biochemical Characters, the Pathogenicity, and the Resistance to Antibiotics of *N. asteroides*.** *Acta Microbiologica Polonica*. 1960, v. 9, No. 4, 343–53.

Nine strains of *Nocardia asteroides* were subjected to a variety of tests and the results are summarized in a series of tables. All the strains proved to be remarkably uniform, the main differences being in the colour and consistency of colonies on various media and pathogenicity for mice. There were also a few differences in their ability to utilize carbohydrates. All the strains studied were morphologically similar, strictly aerobic, catalase-positive, readily killed by heat, long-lived in culture and unable to liquefy gelatin. Their reactions to a variety of antibiotics and chemotherapeutic agents were virtually identical.

In short, strains of *N. asteroides* are reasonably homogeneous, and minor deviations from the norm are no justification for erecting new species. *Ian G. Murray*

VLAKHOV, K. & KARPAROV, M. **Bilateral Pulmonary Aspergilloma and Moniliomata of the Lungs.** *Folia Med.* Plovdiv. 1959, v. 1, No. 4, 217–25. [17 refs.]

The clinical and radiological features of 1 case of bilateral pulmonary aspergilloma and 2 of unilateral pulmonary monilioma are described.

The patient exhibiting bilateral pulmonary aspergilloma, a woman aged 28 years, gave a history of coughing with recurrent haemoptysis, and of an eczematous rash which appeared concurrently on the hands. These episodes appeared to be associated with the menses. Moreover, when the patient became pregnant they disappeared, only to reappear some months after delivery.

On X-ray examination of the lungs it was seen that aspergillomata were present, one in each apical zone. Both showed the fungus mass surmounted by a characteristic crescent-shaped air space separating its upper portion from the cavity wall.

Cultures from the sputum of this patient yielded *Aspergillus fumigatus*.

Although many cases of pulmonary aspergilloma have by now been reported in the literature, case reports of bilateral aspergilloma are rare.

In the 2 other patients, one a man aged 43 years, and the other a woman aged 22, a somewhat similar picture was revealed by X-ray, but the mass was unilateral, in the right apical region in the male patient, and in the left apical region in the female patient.

Candida tropicalis was cultured from the sputum of both these patients. *C. J. La Touche*

STOCKDALE, Phyllis, M. ***Nannizzia incurvata* gen. nov., sp. nov., a Perfect State of *Microsporum gypseum* (Bodin) Guiart et Grigorakis.** *Sabouraudia*. Edinburgh. 1961, Jan., v. 1, Pt. 1, 41–8, 3 figs. & 1 pl. [12 refs.]

This is an interesting and beautifully illustrated account of the structure and development of cleistothecia in a strain of *Microsporum gypseum* derived originally from a human lesion.

Cleistothecia were first observed in this strain 8–10 days after it had been subcultured from freeze-dried material to 4% malt agar. They were a yellowish buff in colour and contained globose to ovate asci in which

were 8 smooth-walled, lenticular ascospores. Cleistothecial initials consisted of a "club-shaped, septate antheridium surrounded by a coiled ascogonium." Investigations of single spore cultures revealed that this species is heterothallic. The materials which provided the best culture medium for the purpose of obtaining cleistothecia were children's hair and chickens' feathers.

The name *Nannizia incurvata* gen. nov., sp. nov. is proposed as the new name for this fungus.

C. J. La Touche

DAWSON, Christine O. & GENTLES, J. C. **The Perfect States of *Keratinomyces ajelloi* Vanbreuseghem, *Trichophyton terrestre* Durie & Frey and *Microsporum nanum* Fuentes.** *Sabouraudia.* Edinburgh. 1961, Jan., v. 1, Pt. 1, 49–57, 4 pls. [19 refs.]

The perfect states of *Keratinomyces ajelloi, Trichophyton terrestre* and *Microsporum nanum* are described in this article and their Latin diagnoses are given for the first time.

These perfect states of dermatophytes were obtained with spore-mycelial suspensions of the given strain or strains by inoculating with them sterilized horse-hair deposited on the surface of unsterilized soil in Petri dishes.

The ascocarps of *K. ajelloi,* namely, *Arthroderma uncinatum* sp. nov. could be produced only by the mating of different strains, showing that this fungus is heterothallic; in *A. quadrifidum* sp. nov. (*Trichophyton terrestre*) the ascocarps can develop from both homothallic and heterothallic mycelia; and again in the case of *Nannizia obtusa* sp. nov. the perfect state of *Microsporum nanum,* they develop only in heterothallic cultures.

C. J. La Touche

Communicable Diseases

The order in this section is:—**Tuberculosis; Venereal Diseases; General Infective Diseases; Other Communicable Diseases.**

For the bacteriology of these diseases see the section on Bacteriology below. For diseases conventionally regarded as tropical, readers are referred to the TROPICAL DISEASES BULLETIN

TUBERCULOSIS

BLACK, J. M. & SUTHERLAND, I. B. **Two Incidents of Tuberculous Infection by Milk from Attested Herds. Public Health and Clinical Aspects.** *Brit. Med. J.* 1961, June 17, 1732–5. [14 refs.]

In July 1959 routine tuberculin testing of a herd of dairy cattle in England revealed 6 reactors. The herd had been attested as free from tuberculosis. The reactors were removed and killed and 1 was found to have tuberculosis mastitis. 2 months later 19 of the cows were found to be reactors and these and a few doubtful reactors were slaughtered; thus the entire herd was extinguished.

In November 1959 a girl aged 5 years was reported to have erythema nodosum and her sister aged 7 was found to be a reactor. The family had been receiving untreated milk daily from the infected herd. The mother, father and the other child were all reactors but showed no other evidence of tuberculosis.

Another family living on the farm had used raw milk. The mother, father and 2 children aged 2 and 4 years were all reactors, but the infant child aged 6 months, who had never been given the milk, was a non-reactor. Members of the farmer's family, who were the only other users of the untreated milk were tested; the mother was a non-reactor, and the father and 2 sons aged 15 and 16 years were all reactors. All reactors in the 3 families were given a 6-months' course of isoniazid and PAS without the occurrence of toxic reactions.

In December 1959 the Medical Officer of Health of the same area was informed that a cow from an attested herd had been killed elsewhere and found to have tuberculosis. The herd had been attested as free from tuberculosis since 1947. The animal had had mastitis in September 1959 after which her milk was used only for calves. The herd was retested and 35 reactors found; none of the calves fed on the milk from the infected cows were reactors. All the reactor animals were killed; 18 were found to have tuberculosis adenitis, and tubercle bacilli of bovine strain were isolated.

Some of the milk from this herd had been sold daily untreated. A list of consumers was prepared and all persons up to the age of 21 who might have consumed the raw milk were tested. Of 160 tested 68 did not react, 23 who had been vaccinated with BCG reacted, 66 not previously recorded as reactors and 3 with a history of being reactors previously reacted. 10 of the vaccinated reactors had hypersensitivity suggesting superinfection.

All the reactors were examined and 85 accepted chemoprophylaxis with isoniazid and PAS but 7 of them failed to take the full course because of various complications. 6 failed to take the drugs regularly and 8 had some upset but persevered.

One child developed a tuberculosis tonsillar lymph node the pus from which showed acid-fast bacilli; tubercle bacilli were not grown on culture. 2 children who had left the village were found to be reactors of whom 1 had enlarged cervical glands and both had enlarged lung

hila. Guineapig inoculation showed evidence of tuberculosis in both cases but no positive cultures of *Mycobacterium tuberculosis* could be obtained.

H. G. Calwell

EMERSON, P. A., BEATH, Gillian & TOMKINS, J. G. **Tuberculosis in Soho.** *Brit. Med. J.* 1961, July 15, 148–52. [10 refs.]

This survey was made in order to discover the incidence and gain information about the genesis of pulmonary tuberculosis in workers in the catering trade in a London Borough. The area chosen (Soho) contains about 400 catering establishments in 1/7 square mile (0·37 sq.km.), and 240 of these were included, *viz.*, 47 public-houses, and 193 restaurants, cafes and coffee-bars.

Cooperation in furnishing lists of workers was obtained from the proprietors of all but 2 establishments, and of the 4,733 workers approached in various ways 2,611 (55%) responded. Before being examined by X-ray each person was interviewed and a questionary was completed concerning personal details.

Of the 2,611 workers examined 86 showed radiological evidence of past or present tuberculosis. 21 were classified as having active disease (6 with positive sputum), 32 had tuberculosis requiring clinic observation only (2 already attending a clinic), and 33 had old healed disease not considered to require observation. The incidences per 1,000 of these 3 categories were 8·0, 12·3 and 12·6 respectively.

Active disease was particularly common in alcohol-servers (at the rate of 12·7 per 1,000) food-preparers (10·6) and other kitchen staff (13·6). Its incidence was surprisingly high in employers and managers (8·6) and lowest in food-servers (6·2). Analysis by country of origin showed active disease in 4 of the 840 workers born in Great Britain (4·8 per 1,000). The incidence in the 1,771 immigrants was 9·6. The Chinese, most of whom come from Hong Kong, had an incidence of active disease of 53·8. Excluding these the rate in the other immigrants was 4·4 compared with 4·8 in those born in Great Britain.

There was evidence that 31 workers had contracted the disease before joining the trade, of whom 11 were from Hong Kong, 6 from Italy and Malta and only 4 from Great Britain. 38 workers appeared to have contracted the disease after entering the trade of whom 26 were immigrants and 12 from Great Britain. Those tuberculous workers born in Great Britain or from areas such as Cyprus, where the incidence of tuberculosis is low, usually join the trade healthy but develop the disease in the first 5 years after joining it in England.

The conclusion reached is that all new entrants to the catering trade in the area concerned should be subjected to X-ray examination, tuberculin-tested and vaccinated with BCG if non-reactors. [A proposal that X-ray examination of the chest should be compulsory for all persons engaged in food trades was rejected in the House of Lords a few months ago on the grounds that tuberculosis is not spread by food. This ground of rejection is ill-based in view of the findings of Emerson and his colleagues.] *H. G. Calwell*

SCHOU, C. **Tuberculosis and Immigration.** *Tubercle.* 1961, June, v. 42, No. 2, 227–32.

Prospective migrants and their families often suffer needless hardship because of questionable signs of tuberculosis, and Schou raises the question whether the present strict immigration regulations concerning tuberculosis are not outdated.

In 1956 some 180,000 Hungarians fled to Austria. Most of them could be moved on elsewhere quickly but 16,226 who remained, having been rejected for emigration, were examined by X-ray. 385 (23·7 per 1,000) were found to have possibly "active" tuberculosis and 388 (23·9 per 1,000) had inactive disease with evidence of fibrosis and calcification. The first group comprised persons with clearly active disease requiring hospital treatment, those with strongly suspected activity and those in whom activity was not excluded by 1 film.

In 1960 353 who had been found to have active or inactive tuberculosis in 1957–58 still remained in Austria. 52 still wished to emigrate and 301 were integrated into the community, nearly all well.

In 1957 Denmark accepted 50 refugees with tuberculosis; 48 of these were at work and self-supporting within 18 months of their arrival in the country. In the period 1950–59 Sweden accepted 1,011 refugees with tuberculosis, mostly from Yugoslavia and Hungary. Only 32 remained in hospital at the beginning of 1960 of whom 26 had arrived in 1958 or 1959. Of 438 about whom information was available, 284 were at work within a year. Only 10% remained unfit for work.

In view of the efficacy of modern treatment and the value to a country of workers, especially if they are skilled, it is Schou's opinion that there could safely be relaxation of immigration regulations with regard to tuberculosis. *H. G. Calwell*

WALKER, P. J. C. **Tuberculosis Movements in relation to Overspill Population.** *Pub. Health.* 1961, July, v. 75, No. 5, 286–97, 1 diagram.

This is a statistical study of the changing rate of notification of pulmonary tuberculosis in an English Urban District into which a large number of people had been moved following slum clearance in a neighbouring city.

As far as was known there had been no intentional selection of the people allocated to the new housing areas, and a survey of their occupational social grading showed them to be fairly representative of the city community of their origin and to approximate to the make-up of the district into which they were moved. The old and new environments were identical geographically and industrially.

In the context of the statistical analysis "prime" notifications refer to cases of tuberculosis arising in original inhabitants of the reception area and "transfers in" refer to cases occurring in the reception area but having originated elsewhere. "Gross" notifications are the sum of these totals for each year.

The population of the Urban District was estimated to be 17,140 in 1949 and 29,620 in 1959. Details of changes in notifications throughout the period were:

	1949	1950	1951	1952	1953	1954	1955	1956	1957	1958	1959
Gross Notifications	8	6	6	12	17	17	16	24	40	39	25
do. per 10,000	4·63	3·43	3·41	6·71	9·32	8·93	7·09	9·83	14·9	14·1	8·46
Prime Notification Rate in City	11·1	8·45	9·44	12·4	13·2	10·0	8·61	11·4	9·82	9·04	6·78
do. in Urban District	4·63	3·43	3·41	6·71	8·75	6·66	5·71	4·92	9·37	9·53	6·44
Transfers In (%)	nil	nil	nil	nil	nil	33	100	100	86·3	66·6	55
Gross Notifications originating from the City (%)	nil	nil	nil	nil	5·9	17·7	18·7	50	37·5	30·9	36

This table provided the initial information that there was a wide discrepancy between the amount of tuberculosis occurring in citizens of the reception area and the gross rate inclusive of the newcomers. Attention is drawn to the year 1957 when there was a gross notification rate of 14·9 in the Urban District. In that year there were 15 transfer cases from the City compared with 6 cases from citizens of the reception area included in the resettled population. New cases were not evenly distributed, there being a large excess in 1 of the 5 new housing estates. Detailed statistical analysis led to the conclusion that the excess of cases actually notified over the expected number was approximately significant.

This experience shows that a massive movement of population can give rise to unexpected problems, and the author recommends that there should be required from every incomer in such circumstances a declaration of chronic ill health so that there may be continuity of the medico-social services which are so important in the treatment and control of tuberculosis. *H. G. Calwell*

STEINBRÜCK, P. Die Tuberkulosestatistik in der DDR. **[The Tuberculosis Situation in the German Democratic Republic]** *Ztschr. f. ärztl. Fortbildung.* 1961, Apr. 15, v. 55, No. 8, Pt. 1, 406–10, 7 figs.

The German Democratic Republic (population 17,300,000 in 1946) has a unified tuberculosis service which embraces both treatment and prevention of tuberculosis and includes rehabilitation.

In 1949 there were 100,000 new cases of tuberculosis and 18,448 deaths but in 1957 the number of new cases had fallen to 23,920 and of deaths to 2,961 of which only 24 were of children under the age of 15 years. This improvement is due to economic betterment as well as to specific measures against the disease.

According to the present trend tuberculosis should cease to be epidemic by 1965. This will happen when the number of new cases in a year falls to 6 per 10,000 with only 1 per 10,000 suffering from an infectious form of the disease.

Statistical information is gained primarily from the register which records patients found to have tuberculosis and the subsequent course of the disease—recovery, relapse or death. Less information is available about the extent of preventive measures such as BCG vaccination and mass radiography.

There was no systematic tuberculin testing until the beginning of the vaccination campaign in 1951–52. Tuberculin surveys of children and young adults mean little because so many are reactors because of BCG vaccination. The reactor rate in adults is not known exactly but the author accepts that nearly all persons over the age of 30 have been infected.

The tuberculosis death rate has been falling and is expected to fall far below 1 per 10,000 by 1965. The present high rate of 1·8 (2·9 in males and 0·95 in females) is due to the relatively high incidence of the disease in older persons which is a heritage of the post-war period. Most of these older patients will die in the next 5 years.

Much effort is being expended on control measures of which mass radiography is the most important after contact examination and supervision of suspects. X-ray examination is not yet compulsory but 10,000,000 persons were examined in 1959 and the yield represented 45% of all new cases diagnosed in that year throughout the Republic.

BCG vaccination has been extended greatly. In 1953, excluding Berlin, 33,888 newborn infants were vaccinated (11·9% of all live births) and in 1959 the number was 257,787 (93·1%). The figures for Berlin were 199,061 (70·8%) in 1956 and 271,955 (93·2%) in 1959. Morbidity from active tuberculosis among persons born in 1937 was just under 2 per 10,000 in the period 1955–58 in those vaccinated with BCG and 33 per 10,000 in 1955 and 27 per 10,000 in 1958 in the unvaccinated.

There has been a considerable fall in morbidity in children and young adults, and tuberculosis is becoming more and more a disease of older persons. In 1949 43·7% of all males with open tuberculosis were aged over 45 and 13·1% over 60. In 1959 the percentages were 71·4 and 33·7 respectively.

Relapse continues to be a serious problem but a slow decline in the number of relapses is going on. It would be worth while investigating whether there is a group of patients with supposedly inactive disease who are at special risk of reactivation and therefore require special observation. It would also be of great advantage to have a criterion for measuring the duration and intensity of supervision to ensure the best results from treatment.

H. G. Calwell

YOUNG, K. **Radiographic Findings in the Chests of 1006 Symptom-Free Candidates for Employment in Somaliland.** *Tubercle.* 1961, June, v. 42, No. 2, 195–8. [11 refs.]

After May 1956 it was required of candidates for government service or the army in Somaliland and of those already in employment, being examined for re-engagement, regrading or overseas service that they should undergo X-ray examination of the chest. The

group could be divided into 4 social classes; scholars for overseas training and senior officials, junior officials and artisans, army and police, and manual workers. Double reading of the skiagrams by one observer was used.

In all 128 (12·8%) of 1,006 candidates X-rayed to May 1960 were recalled for further examination. 50 (5%) were found to have disease requiring treatment. Details are tabulated:

Non-tuberculous disease—20
- Cardiovascular 2
- Respiratory 17 (bronchiectasis 6, bronchitis 4, pneumonia 4, asthma 2, sarcoidosis 1)
- Other 1 (atrophic poliomyelitis 1).

Tuberculous disease—30
- Respiratory 27 (sputum positive 12, sputum negative 7, primary tuberculosis 8)
- Non-respiratory 3 (spinal caries, renal tuberculosis, cervical adenitis).

22 (3·4%) of the cases of tuberculosis were found among the 631 new recruits and 8 (2·1%) among the 376 being examined on re-engagement. There was no consistent relationship with social class.

From the financial standpoint alone this survey was worth while. Tuberculosis is known to be common in Somaliland and these results confirm its high incidence with 3% of the sample having active disease and 1·4% actually expectorating the bacillus. *H. G. Calwell*

STRUTHERS, E. B., LEE, H. K., HAM, S. S., PARK, S. O., PARK, S. J., LEE, K. Y., HONG, J. K. & CHOI, Y. O. **Tuberculosis Contacts in Seoul, Korea. An Analysis of 3,002 Household Contacts, 1959.** *Amer. Rev. Respiratory Dis.* 1961, June, v. 83, No. 6, 808–14, 3 figs.

It is estimated that there are probably more than 600,000 persons with active pulmonary tuberculosis in South Korea (population 23,000,000), and as only 4,000 hospital beds are available for the treatment of such patients supervision at chest clinics and home care are the only practical methods of attacking the problem.

A chest clinic was established in 1954 and others followed so that during the next 4 years 10,668 patients (mostly new) were found with active tuberculosis. From the beginning the homes of the patients were visited by nurses, and by the end of 1959 20,000 visits had been made to 6,000 homes. Treatment was supervised, food was supplied to the destitute and contact examination arranged.

In 1959 in the city of Seoul (population 1,800,000) 3,992 contacts attended the chest clinic but complete data are available for only 3,526 contacts of 900 index cases. 3,002 (85·1%) were X-rayed and 357 (11·9%) found to have active tuberculosis. These were all newly discovered, and 14% were believed to be sources of infection themselves.

In 65% of the diseased contacts the disease was minimal, in 26·3% it was moderately advanced and in only 8·7% far advanced. In the index cases the disease was minimal in 11·8%, moderately advanced in 38·2% and far advanced in 50%.

The discovery rate of active disease in the contacts was 3–5 times that achieved in mass radiography surveys. Overcrowding had a significant influence on the morbidity rate which was also closely related to the extent of the disease and the bacteriological status of the index case, and the duration of exposure.

The source of infection of 86 children with primary disease was their parents in 76, other siblings in 6, grandparents in 6 and unknown in 1. *H. G. Calwell*

BRUCE, R. A. **Observations on the Measurement of Skin Hypersensitivity to Tuberculin.** *Tubercle.* 1961, June, v. 42, No. 2, 199–211, 6 figs. [11 refs.]

"In tuberculin positive subjects there is a linear relationship between the area of skin induration and the log-dose of the intradermal tuberculin injected in a constant volume.

"The area of skin induration is influenced by the volume of injected intradermal fluid as well as the tuberculin dose. A mathematical form is deduced to enable these variations to be predicted.

"A linear relationship is found to exist between the area of skin induration and the dose of infecting organisms. A study of the results occurring with BCG organisms in human subjects and *Mycobacterium tuberculosis* in guinea pigs is used to compare the sensitising ability of these organisms and calibrate the skin reaction in terms of the antigenic stimulus."

WIJSMULLER, G. **Some Implications of the Addition of Tween 80 to Dilutions of PPD Tuberculin with respect to the Study of "Specific" and "Nonspecific" Tuberculin Sensitivity. A Preliminary Report.** *Amer. Rev. Respiratory Dis.* 1961, June, v. 83, No. 6, 815–25.

This work, which was done in Netherlands New Guinea, is concerned with the effect of adding Tween 80 to the phosphate buffer used for diluting PPD. It had previously been found that tuberculins containing Tween 80 were much more potent than had been expected when used in comparative tuberculin studies in the territory, and the object of the present work was to clarify the situation.

The first group studied was in a population living at a high altitude in a district where clinical tuberculosis was unknown. Comparison was made between the sizes of Mantoux reactions to 1 TU of PPD RT 23 (Copenhagen) diluted with Tween and 2·5 TU of RT 23 without Tween. 36 males whose skiagrams did not show pulmonary tuberculosis were tested. The mean reaction to 2·5 TU without Tween was larger than the mean reaction to 1 TU with Tween.

The second group was in a population living at a low altitude in a district where clinical tuberculosis was unknown. Some of the adult males had been out of the district working and might have acquired tuberculous infection. The tests were as in the first group. There was again a larger mean reactivity to 2·5 TU of RT 23 without Tween than to 1 TU with Tween. As compared with the results in the first group the sensitivity to both tests was greater.

The third group consisted of 44 patients newly admitted to hospital with clinical tuberculosis confirmed bacteriologically. The same tests as before were used. In contrast to the findings in the districts where clinical tuberculosis was unknown the reactions to both tests were of approximately the same size. There was some indication that reactions to 1 TU with Tween might have been slightly larger than those to 2·5 TU without Tween.

The fourth group was drawn from the general population of a coastal district where clinical tuberculosis is common. 376 persons were tested as before. Persons with small and medium reactions (up to 12–15 mm.) to 1 TU with Tween had larger reactions to 2·5 TU without Tween, but persons with strong reactions to 1 TU with Tween (16 mm. or more) had reactions of approximately the same size to 2·5 TU without Tween.

Previous comparative tuberculin testing had led to the conclusion that in the district from which the second group was drawn non-specific sensitivity was universal. Accordingly 118 persons were tested with 20 TU of RT 23 with Tween and 50 TU without Tween. No severe reactions occurred, and it was seen that the reaction to 50 TU without Tween was stronger than that to 20 TU with Tween.

Human PPD-Seibert was used in another second group sample when duplicate tests were given with 5 TU without Tween and 2 TU with Tween. 143 persons were tested, and it was found that the reaction to 5 TU without Tween was somewhat stronger than to 2 TU with Tween. The same tests were given to 27 patients with bacteriologically confirmed pulmonary tuberculosis. The reaction to both tests was much the same, 2 TU with Tween giving somewhat larger reactions than 5 TU without Tween.

In the last study 153 persons living on an island where mass radiography had revealed presumed active tuberculosis in 1·7% were tested with 5 TU of PPD-S without Tween and 2 TU of PPD-S with Tween. The large reactions tended to be of the same size with both tests whereas persons with smaller or medium reactions to 2 TU with Tween had larger reactions to 5 TU without Tween.

It is concluded that the addition of Tween to the diluent of human PPD enhances the reaction in persons infected with true tubercle bacilli and is therefore advantageous in the search for such persons. The distribution of reactions by size will show a better separation between persons specifically and those non-specifically infected. In the study of non-specific sensitivity, however, the persons specifically and those non-specifically infected. in the study of non-specific sensitivity, however, the addition of Tween is a disadvantage, and it seems better to continue to use as diluent a phosphate buffer not containing Tween. *H. G. Calwell*

LIN, Sung-Cheng. **Studies on Detection of "Complete" and "Incomplete" Antibodies in Tuberculosis with Sheep and Chicken Red Blood Cells as Antigen Carriers.** *Fukushima J. Med. Sci.* 1959, Dec., v. 6, Nos. 3/4, 235–52, 2 figs. [13 refs.]

DAVIES, P. D. B. **The Natural History of Tuberculosis in Children. A Study of Child Contacts in the Brompton Hospital Child Contact Clinic from 1930 to 1952.** *Tubercle.* 1961, Mar., v. 42, Suppl., 40 pp., 12 figs. on 6 pls. [13 refs.]

It is rather a pity that the complete account of the work of the Child Contact Clinic could not be published at the same time as a similar investigation reported by BRAILY as part of the Harriet Lane Study in Baltimore, U.S.A.; the two reports are complementary both in the similarities and differences in the conclusions. The Brompton report deals with 1,567 children who were found to be infected with tuberculosis in the years 1930–52; hence it closes before antimicrobial drugs came into common use, and, by complicating the picture, made such a study as this impossible in the future. The object of the investigation, initiated by the Brompton medical staff with the late Dr. R. C. WINGFIELD as prime mover, was to investigate the natural history of tuberculosis from childhood to adult life. The investigation was carried out by a succession of workers under the supervision of Dr. W. E. Lloyd and Dr. Margaret Macpherson. The data have been correlated and reported on by Dr. P. D. B. Davies and the report has the approval of the Brompton Hospital Research Committee.

Of the 1,567 children, nearly 50% developed radiological or clinical evidence of tuberculosis, but the age pattern was not uniform; among the infants 75% had evidence of active tuberculosis and 25% died; in adolescents the figures were 40%, with 2% dying of the disease. The type of disease showed a corresponding difference. Disseminated lesions appeared in nearly half of the infected infants, whereas among the 535 children who were infected in adolescence only 1·5% showed evidence of such lesions.

When the investigation was started the most stringent criteria were laid down for the diagnosis of calcified lesions. Hence the observation that 10% of calcified lesions noted at the first visit turned out to be active, is of considerable significance. On the other hand no uncalcified lesions were proved to be healed.

Particular attention was paid to segmental lesions. Marked enlargement of lymph node was much commoner in infants, and this taken in conjunction with the difference in anatomy of the bronchi led to the development of segmental lesions, which accounted for 32% of all pulmonary lesions in children infected before the age of 1 year, against 7% in children infected after the age of 10. The contents of many of the tuberculous bronchial glands must be coughed up as calcification became visible in 90% of the primary lesions but was only present in the glandular components in 75%. Contrary to some other reports the prognosis for these segmental lesions was good, for in only one patient had an episode of infection appeared as the result of residual anatomical abnormality, and this child developed adult type of tuberculosis; but against this, 8 years after the investigation had closed, it was found that 7 had required surgical treatment, 5 for lower lobe bronchiectasis.

Comparison between the Brompton figures and those of other workers in Great Britain [this *Bulletin*, 1947, v. 22, 688; 1953, v. 28, 325; 1956, v. 31, 1080; 1957 v. 32, 1037] shows that there was often a considerable difference

in the findings, but careful investigation into the methods of assessment and selection of patients would probably go a considerable way to explaining many of the divergencies. Considering the great movement of population and dispersion of London children owing to the war the high percentage of children with whom contact has been retained reflects great credit on the Brompton workers. This study will take its place as a classic among the long-term research investigations into the natural history of tuberculosis. Read *in extenso* it will be of the greatest interest to workers in the field which it covers. *F. H. Young*

SILVER, C. P. & STEEL, S. J. **Mediastinal Lymphatic Gland Tuberculosis in Asian and Coloured Immigrants.** *Lancet.* 1961, June 10, 1254–6, 4 figs.

Since the end of the last war there has been a considerable increase in the numbers of immigrants to the United Kingdom from Asia, Africa and the West Indies, who now number 200,000. This report on 7 patients who had mediastinal lymphatic gland tuberculosis and who came from India and the West Indies is of considerable interest. The 7 patients presented with considerable pyrexia, cough and sputum, and the illness was long, with a tendency to relapse. X-rays showed obvious enlargement of the hilar glands, unilateral in 3 patients, and bilateral in one. The paratracheal glands were enlarged on the right side in 2, and with bilateral enlargement of the upper mediastinal glands in 1. Considerable difficulty was found in obtaining tubercle bacilli from the sputum in these patients when they first presented. At first the mediastinal gland enlargement was usually unaccompanied by associated parenchymal lesions. The response to the standard antituberculous treatment was poor, X-ray changes being very slight. Usually within a relatively short time involvement of the lung parenchyma occurred, and this responded very much better to the antituberculous drugs.

The authors provide evidence which seems to show that the conditions described are not exactly similar to primary tuberculosis as it occurs in children in Great Britain. Apparently in these patients the enlargement of the glands due to tuberculosis took place at a considerably later date than would have been expected in English children. They suggest that these patients failed to acquire resistance at the time of infection, thus giving a clinical picture presenting features of primary and chronic pulmonary tuberculosis simultaneously. Unless this condition is borne in mind considerable difficulties in diagnosis are apt to occur; in 1 patient carcinoma was so confidently diagnosed that X-ray treatment was applied. *F. H. Young*

KAGRAMANOV, A. I., MAKARÉVITCH, N. M., OSSINTSEVA, V. P., PAPORISH, C. D. & GONLEVICH, M. [La tuberculose des noeuds lymphatiques du cou de l'enfant, provoquée par des mycobactéries tuberculeuses du type "avium"] **[Tuberculosis of the Cervical Lymph Nodes in a Child Caused by Tubercle Bacilli of Avian Type]** *Problemy Tuberkuleza.* 1961, v. 39, No. 1, 54–61, 6 figs. [In Russian.] French summary.

The authors describe the case of a boy aged 11 years who was admitted to hospital in 1959 with a diagnosis of tuberculous cervical adenitis. The graduated tuberculin test was negative at all dilutions and the intradermal test was weakly positive with the second dilution; no tubercle bacilli could be seen in stained preparations of pus from the affected glands, but atypical mycobacteria could be isolated in culture. The patient was taken home against advice, and when readmitted after 7 months a slow progression of the condition could be observed, with an increase in the strength of the reaction to intradermal tuberculin. A more marked reaction was obtained with tuberculin prepared from avian tubercle bacilli. Treatment with PAS and streptomycin for 1 month was ineffective. Cultures of pus on Petragnani medium gave a growth of fine moist colonies within 21 days, and after 4–6 days on subculture. The morphology of the organisms was atypical. They were of low virulence for guineapigs and mice, but highly virulent for rabbits and chickens. On the basis of the cultural characteristics and animal pathogenicity the organisms were considered to be tubercle bacilli of avian type. *D. J. Bauer*

LANCET. 1961, July 1, 14–16. **Aetiology of Erythema Nodosum in Children. A Study by a Group of Paediatricians.**

82 new cases of erythema nodosum in children in Sheffield and other centres in England were studied from the point of view of tuberculous and streptococcal infection. In children under 5 years tuberculosis was found to be the commonest cause, although cases were rare. In children aged between 5 and 10 years active tuberculosis was present in 38%, but in children over 10 years in only 11%. Streptococcal infection was the commonest cause after the age of 5 but in some cases a double aetiology could not be excluded. *A. B. Christie*

SALIBA, A., PACINI, L., DOWDEN, C. W. & BEATTY, O. A. **Initial Chemotherapy in Pulmonary Tuberculosis: Daily Streptomycin with High Isoniazid Dosage in previously Untreated Cases.** *Acta Tuberculosea Scandinavica.* 1961, v. 40, No. 2, 113–25, 1 graph & 4 figs. on 9 pls. [18 refs.]

The investigation reported in this paper commenced as a comparison between patients treated with high doses of streptomycin daily and high doses of isoniazid, and a group of patients in whom the isoniazid dosage was conventional. The comparison had to be dropped as it was found the patients in the high isoniazid group were on the whole initially considerably worse than those in the low isoniazid group. In both groups of patients 1 gm. streptomycin was given daily. In the high isoniazid group there were 42 patients and in the low isoniazid group there were 15. At the end of 6 months, sputum conversion was obtained in 100% in both series. The X-ray improvement was rather better in the high isoniazid group, and sputum conversion occurred earlier in the high isoniazid group than in the other.

Little in the way of toxic reactions were reported from the daily use of streptomycin but the age of the patient

is not reported. Vestibular disfunction was only noted in 3 out of the total number of patients. The use of pyridoxine prevented frequent toxic reactions to isoniazid.

The authors contend that while their paper is a little in favour of high doses of isoniazid the important finding is the value of the use of the daily dose of 1 gm. streptomycin. They express surprise that in spite of the many reports that intermittent streptomycin is apt to lead to failure this method of treatment is still adopted.

F. H. Young

VELU, S., ANDREWS, R. H., ANGEL, J. H., DEVADATTA, S., FOX, W., JACOB, P. G., NAIR, C. N. & RAMAKRISHNAN, C. V. **Streptomycin plus Pyrazinamide in the Treatment of Patients excreting Isoniazid-Resistant Tubercle Bacilli, following Previous Chemotherapy.** *Tubercle.* 1961, June, v. 42, No. 2, 136–47. [23 refs.]

This paper presents the results of 1 year's treatment with streptomycin and pyrazinamide of 69 patients (in Madras, India) with active tuberculosis in whom earlier drug treatment had failed. All were excreting tubercle bacilli which were resistant to isoniazid but sensitive to streptomycin. As far as was known none of the patients had previously been treated with streptomycin or pyrazinamide. After the exclusion of 12 patients for various reasons there remained 57 for study of whom 30 had received isoniazid and PAS previously and 27 isoniazid alone.

The standard regime comprised 1 gm. of streptomycin daily on 6 days each week with pyrazinamide 1–1·5 gm. daily every day. Variations from the standard were made in individual patients; 14 patients received part of the treatment in hospital and the remainder wholly as out-patients pursuing their normal activities.

The patients were aged 17–64 years, 30 were males and 27 females, and the disease was advanced in the majority only 5 (9%) not showing cavitation. 1 patient died at 3½ months, and treatment was stopped in 20 patients between the 5th and 10th months because of failure. In 1 other it was stopped after 8 months because of irregular attendance; his disease was inactive at 1 year and he was included in the analysis of results.

Of 52 patients with initial cavitation 12 (23%) showed none and 20 (38%) less at 6 months. Disappearance of cavitation was noted mainly in patients in whom it had been slight at the start. 5 patients had no cavitation at the start, and were still without it at 6 and 12 months. In the 51 patients assessed at 12 months cavitation had disappeared in 16 (31%) and was less in 9 (18%). It did not disappear in any patient in whom it had been extensive initially.

There was a rapid fall in the bacterial content of the sputum in the early months. At 1 month all the cultures in 42% of the 57 patients were negative. This proportion rose to 75% at 2 months but fell to 60% at 3 months. Excluding the patients whose treatment was changed because of an unfavourable response the cultures were negative in 63% at 6 months, 58% at 9 months and 68% at 12 months.

A total of 25 patients yielded streptomycin-resistant strains, 6 for the first time at 1 month, 10 at 2 months, 5 at 3 months, 2 at 4 months, 1 at 7 months and 1 at 8 months. Reliable results of tests for sensitivity to pyrazinamide are not available.

At the end of 1 year 32 (56%) of the 57 patients had bacteriologically quiescent disease, 4 patients had relapsed bacteriologically, the disease had remained active in 1, and 18 patients who had continued to excrete bacilli had had their treatment changed. 1 patient had an isolated positive culture at 10 months and 1 patient died.

The patients' co-operation was satisfactory and the regime well tolerated. The authors consider this combination of drugs a valuable one for patients in whom earlier chemotherapy has failed.

H. G. Calwell

GORDON, C. G. I. **A Method of Controlled Home Treatment of Pulmonary Tuberculosis in Tanganyika.** *Tubercle.* 1961, June, v. 42, No. 2, 148–58. [14 refs.]

The area of Tanganyika Territory in which this work was done is over 45,000 square miles with a population of 800,000 living in primitive, overcrowded and unhygienic conditions. Tuberculosis is common in Tanganyika, and Gordon has estimated that there are at least 52,000 persons with active disease requiring treatment. The problem can best be met by home treatment, a scheme of which is described in the paper.

The present method was adopted in 1957 after the co-operation of the chiefs and headmen had been sought and the nature of tuberculosis and the proposed plan explained. They were told that they could best help by tracing defaulters, warning those found not to be taking their drugs regularly and ensuring that patients did not frequent crowded meetings and drinking houses.

African tuberculosis home visitors were trained in case finding, instruction of patients and their families, tuberculin testing of families and other contacts, dispensing of medicines, simple examination, and urine testing to see if PAS were being taken. They were based on all available rural general dispensaries.

An assessment clinic with an X-ray plant was set up in each of the 2 main towns, and all patients were expected to attend the nearest main clinic every 3 months. Those who were destitute were given free transport.

All new patients were kept in hospital for 1–3 months at the start. Intercurrent diseases were treated and specific chemotherapy was given for the tuberculous condition consisting of daily streptomycin and isoniazid. Individual health education was given. After completion of the initial treatment those who were considered to have made satisfactory progress were sent home if the conditions were suitable, and treatment with isoniazid and PAS was continued under the supervision of the home visitor. After 3 months' home treatment the patient came to a main clinic for assessment. If he was doing well, treatment at home for another 3 months' period was prescribed, and this process was repeated every 3 months until the disease was considered to be inactive. Thereafter assessments were made at less frequent intervals.

Urine examinations showed that 41 of 94 patients (44%) had a negative test for PAS on at least 1 occasion;

28 (69%) of these had a negative test on only 1 occasion, 9 on 2–4 occasions and 4 on 5 or more occasions.

100 patients first admitted in 1957 with sputum-positive pulmonary tuberculosis have been followed up for 3 years. 3 had died (1 from haemoptysis, 1 from eclampsia and 1 in child-birth), and 2 had been lost sight of. The results in the remaining 95 were:

General condition	improvement	slight	1
		moderate	5
		marked	89
Sputum (direct)		positive	1
		negative	94
X-ray findings		virtual resolution	31
		slight residue	32
		moderate residue	23
		severe residue	9

89 patients were considered fit for their normal occupation (agriculture) at the end of the period.

H. G. Calwell

BELL, W. J., BROWN, P. P. & HORN, D. W. **Prolonged out-Patient Chemotherapy of Pulmonary Tuberculosis in West Africans following Short-Term Hospital Treatment.** *Tubercle.* 1961, June, v. 42, No. 2, 159–68, 1 fig. [25 refs.]

In Ashanti, Ghana, where this work was done, most cases of pulmonary tuberculosis are found among adult male peasants from the rural areas. The disease is usually extensive and acute or subacute, hospital beds are insufficient and facilities for thoracic surgery do not exist. Definitive treatment has therefore to be given entirely outside hospital or after a short stay in hospital; moreover it must be largely oral.

The investigation was confined to adult male West Africans with X-ray evidence of acute or subacute pulmonary tuberculosis involving more than 1 lung zone, not previously treated for more than 14 days and expectorating tubercle bacilli sensitive to the drugs employed.

Those eligible were admitted to hospital and allocated at random to 1 of 2 treatment groups: group SPH—streptomycin, isoniazid and PAS daily for 12 weeks in hospital and (without streptomycin) for 9 months at home; group SH—streptomycin and isoniazid daily for 12 weeks in hospital and isoniazid and PAS for 9 months at home. Intercurrent diseases were also treated.

159 patients were admitted, 78 to the SPH and 81 to the SH group. 91 were lost from the study (2 by death in the first 3 months) for various reasons stated. The groups were well comparable at the start in respect of clinical, radiological and bacteriological state but less so in respect of extent and nature of the lesions.

Throughout the period of treatment progress as judged clinically and radiologically was almost parallel in the 2 groups and at the end of 12 months there was little to choose between them. During the earlier months of treatment the SPH regime cleared bacilli from the sputum more quickly and cavities closed more quickly also. Changes in general condition were almost the same in both groups, and at the end almost all patients were in good condition.

After 3 months over two-thirds of the SPH and ove one half of the SH group had negative sputum smear Irrespective of the regimen used 30% of all patients le hospital expectorating acid-fast bacilli, and after months' treatment 2 SPH and 9 SH patients still ha positive smears. After the 6th month there was littl difference; there was no significant difference in th proportion in either group with a still positive sputum

In the SPH group 2 cultures showed partial resistanc to streptomycin and later negative cultures, but eac patient was lost sight of. In the SH group 5 develope resistance and were removed from the study according t the protocol.

It was concluded that either of these regimens reasonably effective but considering the high rate c default and the failure of many patients to take PA there are serious limitations to the definitive usefulnes of the out-patient chemotherapy of pulmonar tuberculosis in a community such as that described.

H. G. Calwell

COHEN, R., KALSER, M. H. & THOMSON, R. V. **Fata Hepatic Necrosis Secondary to Isoniazid The rapy.** *J. Amer. Med. Ass.* 1961, June 10, v. 17 No. 10, 877–9, 1 fig.

By 1960, 6 cases of jaundice suspected of being du to isoniazid therapy in patients receiving average thera peutic doses were reported [see, for example, th *Bulletin*, 1959, v. 34, 750] but in all of these potentiall hepatotoxic drugs such as streptomycin and PAS wer also given. This report describes a case of fulminatin sub-massive necrotic hepatitis associated with isoniazi administration.

The patient, a 50-year-old Negro had suffered for th previous year with diabetes mellitus and sarcoidosis wa subsequently diagnosed, confirmed by a skin nodul biopsy. The patient was treated with methylprednisolon (Medrol), 6 mgm. daily, and isoniazid, 300 mgm. dail with a good result. After about 2 months' administratio the patient was admitted with jaundice associated wit an enlarged and tender liver. Full pathological data ar given. The isoniazid was stopped, but 20 mgm. c prednisone daily were given. At the end of 2 months th patient's liver was no longer palpable and he wa asymptomatic. After discharge the isoniazid therapy wa re-started at another hospital and the patient was re admitted after a month's treatment. His jaundice ha recurred and the isoniazid was continued and he wa treated with 2 mgm. of methylprednisolone 3 times dail 2 gm. of tolbutamide 3 times daily, 15 ml. of aluminium hydroxide gel with magnesium hydroxide 4 times dail and 2·5 mgm. of trimeprazine tartrate (Temaril) 4 time daily. On the 9th day in hospital the patient was i impending hepatic coma, and 200 mgm. of hydrocortison sodium succinate intravenously was added to the dail therapeutic programme. The liver become no longe palpable and the patient rapidly deteriorated and died o the 14th day. The material obtained by percutaneou liver biopsy was similar to that appearing in vira hepatitis, and the findings at autopsy were those c massive necrosis resembling those seen in overwhelmin viral hepatitis. Although the diagnosis of relapsing serum

hepatitis cannot be completely disproved or the possible contributory role of the tolbutamide and prednisone, the time relationship, the use of the isoniazid, and the occurrence of the hepatitis makes it highly probable that its cause was isoniazid. *F. H. Young*

HILLERDAL, O., HINT, V. & SJÖGREN, I. Tuberkulosterapi och resistens. [**Drug Resistance in Tuberculosis**] *Nordisk Med.* 1961, June 22, v. 65, No. 25, 902–5.

The English summary appended to the paper is as follows:—

"A review is given of some actual problems regarding the clinical significance of drug resistance in tuberculosis, and the method used at Uppsala for testing drug resistance in tuberculosis is briefly described.

"180 patients with active tuberculosis were treated in the University Lung Clinic at Uppsala, Sweden, over the period July 1, 1959—June 30, 1960. Tubercle bacilli were found in 88 patients, i.e. 49 per cent. In 63 of these the resistance of the tubercle bacilli to streptomycin, PAS and isoniazid was examined immediately after admission to hospital.

"'Primary' resistance—among patients previously not treated with antituberculous drugs—was demonstrated in 1 of 31 cases. The tubercle bacilli of this patient were resistant to all of the three drugs.

"32 patients had previously received antituberculous treatment. Resistance to at least one drug was found in 18, to at least two drugs in 8 and to all of the three drugs in 4 of these patients.

"Of 63 examined patients 15 were resistant to isoniazid, 9 to streptomycin and 9 to PAS."

FORBES, G. B. **Non-Reactive Tuberculosis in a Cortisone Treated Patient.** *Tubercle.* 1961, June, v. 42, No. 2, 233–40, 6 figs. [10 refs.]

Occasionally case reports are published of a rare form of tuberculosis characterized by widespread occurrence of necrotic lesions containing vast numbers of tubercle bacilli, normal reaction of the body to the tubercle bacilli being absent. This has been called non-reactive tuberculosis. The main tissues affected are the reticulo-endothelial system, with little or no involvement of the kidneys, lungs, or meninges; frequently it is associated with serious haematological disease. It is almost invariably fatal and the true diagnosis is usually established only after death.

This paper reports such a case. A woman aged 55 became unwell in February 1958, with a feverish illness associated with cough and sweating at night. She had previously suffered from recurrent bronchitis. In August 1958, her right calf was painful and swollen; this deep vein thrombosis extended into her thigh. Her temperature persisted and moderately severe hypochromic and microcytic anaemia was found with a leucopenia. X-rays taken on the 24th April, 1959, showed a calcified focus in the left lower lobe and rather large hilum shadows. A film taken 2 months later showed obviously enlarged hilar lymphatic glands. The patient was thought to be suffering from systemic lupus erythematosus in spite of the absence of L.E. cells. Triamcinolone was given in doses of 4 mgm. 4 times a day with dramatic improvement. Pyrexia soon returned, her general condition deteriorated and she died about a year and a half from the time she first became ill. At autopsy enlarged glands in the thorax and abdomen were found completely replaced by a homogenous white tissue of the consistency of processed cheese. There was no naked eye evidence of tuberculosis in the lungs. Extensive suppurative pyelonephritis involving the whole of both kidneys was found. Vast numbers of tubercle bacilli were found in the glands with very little reaction; simliar appearances were found in the liver and spleen.

It was thought that the corticosteroids may have influenced the disease but it must have been present before these were used because of the presence of enlarged glands in the radiograph of the lung. Possible causes of this uncommon condition are discussed.

F. H. Young

LOUGHLIN, J. F. **Miliary Tuberculosis following Prolonged Therapy with Prednisone.** *Southern Med. J.* 1961, June, v. 54, No. 6, 670–72. [14 refs.]

This article reports the development of miliary tuberculosis in a coloured man who had been treated with corticosteroids for chronic exfoliative dermatitis for 3 years. There is a full report of the findings, and the diagnosis of miliary tuberculosis at first was difficult, but when once made treatment by antituberculous drugs was successful. The author points out the importance of bearing miliary tuberculosis in mind, especially so when disseminated lupus erythematosus is present.

F. H. Young

VON HOLST, H., PEGELOW, K. O. & STERKY, G. **The Prognosis for Diabetics with Pulmonary Tuberculosis.** *Acta Tuberculosea Scandinavica.* 1961, v. 40, No. 2, 157–70, 2 figs. [22 refs.]

This paper studies 150 patients who had pulmonary tuberculosis and diabetes mellitus. They were observed during 3 periods: 1936–45; 1945–50, and 1950–55. The follow-up was 5 years. In the first period there was no antimicrobial treatment; in the second, little or unsatisfactory methods were used; in the third period more or less standard treatment was the rule.

Males outnumbered females by 2 to 1, and the age-groups varied in the 3 series, there being a pronounced shift to the older age-groups in the third series. The number of diabetic patients with pulmonary tuberculosis who had passed the age of 50 had approximately doubled and was greater than that for non-diabetics.

Mean duration in each period of the existence of the diabetes before the onset of pulmonary tuberculosis was 8 years. The time relationships of the respective onsets showed that it was quite evident that tuberculosis was a complication of diabetes and not *vice versa.*

In the first series at the end of 5 years the mortality rate was nearly 50%, whereas in the third period the rate was 14%. The mortality in each series was highest during the first year after the onset. When the working

capacity was studied, it was found that 12 (21%) were fully fit in the first period, 10 (25%) in the second, and 22 (43%) in the third. In the third period surgery was undertaken in 18 patients, with 1 death from tuberculosis, and at the end of 5 years 12 were fully fit for work.

The authors state that they do not think that their paper helps in deciding whether meticulous treatment of the diabetes has much effect on the pulmonary tuberculosis.

[See also this *Bulletin*, 1958, v. 53, 1120.].

F. H. Young

ARJUNDAS, G. & SUBRAMANIAM, R. **Tuberculous Meningitis: a Review of 51 Cases in Madras.** *Tubercle.* 1961, June, v. 42, No. 2, 187–94 [14 refs.]

51 patients aged 10 years or over were admitted to hospital in Madras between September 1957 and December 1959. The criteria of diagnosis were clinical evidence of meningitis, positive cytological and biological findings in the cerebrospinal fluid and the absence of any other pathogenic organisms in smears and cultures of the fluid. The diagnostic demonstration of acid-fast bacilli in the fluid was not attempted often owing to the absence of adequate facilities.

Of the 51 patients 29 were males and 22 females; 42 were under 40 years old, 9 were over 40. 23 patients (4 deaths) were in stage I, *i.e.* with little or no clinical sign of meningitis and the diagnosis established mainly by abnormal fluid; 4 (1 death) were in stage II, *i.e.* between stage I and stage III; and 24 (13 deaths) were in stage III, *i.e.* extremely ill, deeply comatose, with gross pareses. The duration of illness before diagnosis did not seem to be closely correlated with the stage of the disease on admission.

44 patients were examined thoroughly for evidence of other tuberculosis. Miliary disease was found in 3, active pulmonary tuberculosis in 4 and tuberculous otitis media in 1. 34 patients (66·6%) had disturbance of higher cerebral function. Those admitted in deep coma fared worse than others. 14 patients showed evidence of cranial nerve palsy, most commonly involving the oculomotor nerve. 12 had some form of other motor paralysis.

At the beginning convulsions were seen in 10 (19·6%) of whom 5 died, 4 recovered completely, and 1 has been put on long-term anticonvulsant drugs. Headache was present in all conscious patients and was one of the earliest symptoms. Photophobia was common but very few patients complained of vomiting.

Meningism was present in 40 of 50 patients specially examined for it. Choroidal tubercules were not seen in the 28 patients examined for them. The authors mention that ability to detect such tubercles probably varies with experience.

The protein content of the cerebrospinal fluid was found to be directly proportional to the severity of the disease. The chloride and sugar contents were low. Acid-fast bacilli were seen in the fluid of 3 of the 10 examined intensively. 4 of 7 patients tested (Mantoux 100 TU of OT) were found to be reactors.

The patients were selected for 3 main types of treatment according to their condition. The regimes were (1) intramuscular streptomycin, oral isoniazid and intravenous (later oral) PAS, (2) the same plus corticosteroids and (3) regime 2 plus intrathecal streptomycin. The results were:

	Stage I		Stage III	
	Total	*Deaths*	*Total*	*Deaths*
Group 1	9	0	13	7 (54%)
Group 2	7	2	6	5 (83%)
Group 3	7	2	5	1 (20%)

There was 1 death in the 4 patients in stage II.

A follow-up of the 34 survivors was attempted but only 8 attended. 1 had had 2 relapses, 1 was mentally deranged but showed no evidence of activity of the disease. His mental condition became normal after withdrawal of isoniazid; 1 had bilateral nerve deafness and ataxia and 5 were well. *H. G. Calwell*

YOUMANS, G. P., PARLETT, R. C. & YOUMANS, Anne S. **The Significance of the Response of Mice to Immunization with Viable Unclassified Mycobacteria.** *Amer. Rev. Respiratory Dis.* 196 June, v. 83, No. 6, 903–5. [Refs. in footnotes.]

Studies in tuberculin sensitivity have shown that a high proportion of the people in many areas of the United States of America have been infected by atypical mycobacteria [this *Bulletin*, 1960, v. 35, 132]. The question is asked whether such infection confers increased immunity to later infection by virulent human tubercle bacilli.

The authors have carried out experimental studies to measure the immunizing power of representative cultures of unclassified mycobacteria. Mice were inoculated intraperitoneally with different numbers of young viable cells of *Mycobacterium kansasii* (a photochromogen), of a scotochromogen bacillus, of 2 strains of the Battey bacillus, of *Mycobacterium avium* and of a strain described as "rapid grower". 28 days later these mice were inoculated intravenously with a culture of the H37Rv strain of *Myco. tuberculosis*, and the immunizing efficacy was determined by noting the proportion of each group which survived 30 days.

At 4 and 8 weeks after vaccination 5 vaccinated but unchallenged mice were killed and examined for gross signs of disease produced by the viable unclassified mycobacteria used for vaccination.

The results were analysed. It was found that a high degree of immunity to virulent superinfection developed only in those animals vaccinated with *Myco. kansasii* and the Battey bacillus. The effectiveness of *Myco. kansasii* approached that of BCG [*ibid.*, 1958, v. 33, 268] and may have been related to the presence of pulmonary lesions in the mice vaccinated with this strain (suggesting *in vivo* microbial multiplication). The Battey strain conferred immunity of lesser degree but similar to that conferred by strain H37Ra and *Myco. avium*. The scotochromogen conferred only slight immunity and the rapid grower none.

"In view of these results and of the apparent widespread occurrence of inapparent infection in human beings with these unclassified mycobacteria, it has been suggested that a large human population may exist

the United States nonspecifically naturally immunized against infection with *M. tuberculosis*. The suggestion has also been made that this situation may have played a large part in the rapid decline in tuberculosis morbidity . . .". *H. G. Calwell*

MOLLOHAN, C. S. & ROMER, Mary S. **Public Health Significance of Swimming Pool Granuloma.** *Amer. J. Pub. Health.* 1961, June, v. 51, No. 6, 883–91, 5 figs.

This is a study of 262 cases of " sore elbow " or swimming pool granuloma, a disease previously identified in Sweden as due to the acid-fast bacillus *Mycobacterium balnei* [this *Bulletin*, 1954, v. 29, 1186].

In June 1959 a dermatologist reported several cases of lesions on the elbow, some of which were sufficiently severe to require skin grafting, following swimming in a mineral water pool. Investigations then made by the Colorado State Department of Public Health brought to light many further cases.

The early lesions began typically as a reddish papule the size of a rice grain 3 to 4 weeks after swimming in the pool. The lesion grew to the size of a pea in about 2 weeks and became hardened and purplish in colour. It might open and drain, then become covered by crusts under which there was a shallow area of ulceration. Healing tended to be spontaneous over a period of a few months to 2 years leaving a soft, shiny scar.

Bacteriological examinations of biopsy specimens, samples of the pool water and silt from the bottom, and swabs from the sides of the pool, led to the isolation of *Mycobacterium balnei*.

There is a description of the swimming pool and of the sources of the pool water.

All the 262 cases were in whites, of whom 143 were female and 119 male. 86% of the cases were in patients between the ages of 10 and 19 years. The elbow was the site of the lesion in 85% of cases although the condition was also found on the knee (20 cases) and occasionally on the foot, ankle, finger and leg.

Some interesting work was done as the result of a report from Sweden that 24 patients with swimming pool granuloma had given a positive tuberculin reaction although they had been tuberculin negative before the lesions developed. In the present study of 185 persons with granulomatous lesions who were tested (Vollmer patch test) 151 (82%) showed positive tuberculin reactions, 77% of these having converted since their last previous patch test 1 to 2 years before. The patch test was also done on 1,648 children in the community with the result that 4·3% of those with no skin lesions gave a positive result compared with 82% for those with lesions.

There is a good discussion. *M. E. Delafield*

VENEREAL DISEASES

HARRISON, L. W. **History of the Medical Society for the Study of Venereal Diseases; the First Thirty Years, 1922–1952. With a History of the Scottish Branch by R. FORGAN.** *Brit. J. Venereal Dis.* 1961, Mar., v. 37, No. 1, 2–32.

The title of this article is self explanatory. The birth of this society (MSSVD) in 1922 is attributed to Dr. David WATSON but throughout its life its guide, counsellor and friend has been Col. L. W. HARRISON. The Brussels Agreement of 1902, the Royal Commission of 1913 and the Public Health Regulations (Venereal Diseases) of 1916 together with the great increase of venereal disease during and after the first world war all combined to indicate the need for such a society as the MSSVD. The first president was Dr. David Watson with Dr. E. R. T. CLARKSON as secretary and treasurer; these together with a provisional committee of 5 drafted the aims and rules of the society (Dr. R. FORGAN had previously drafted a tentative constitution). Details are given of the early general meetings (1922–1924), research activities and the inauguration of the *British Journal of Venereal Diseases* published at first by commercial firms. This last was a great success and a considerable source of income to the Society until 1946 after which publication was undertaken by the British Medical Association.

Membership of the Society varied between 302 and 150 and in 1951 was 262. A note on the Scottish Branch by Dr. Forgan is included; the first president was Mr. David LEES and first secretary Dr. Robert Forgan; this branch flourished at first, relapsed in 1942 and was resuscitated in 1954 by Dr. Robert LEES. In appendices are given papers read to the Society 1922–1952, a list of officers and Members of Council and Editors and Assistant Editors of the Journal. The composition of this article must have been a Herculean task and could have been undertaken by no one more suitable than Col. Harrison, whose name is still one to conjure with in the world of veneral diseases. *T. E. Osmond*

THOMAS, C. G. A. **The Light of Many Minds.** *Brit. J. Venereal Dis.* 1961, Mar., v. 37, No. 1, 33–58. [Numerous refs.]

This is such a scholarly, masterly and philosophical approach to the subject of veneral diseases that it seems almost an impertinence to try to condense some 27 pages into a few hundred words. The object is to survey the scientific basis of venereology with special reference to other branches of medicine. The word venereal must be given the widest meaning and it must be accepted that venereal diseases are as old as man and have been recorded as far back as history goes. The development of morbid anatomy first (1505) caused venereal disease to be firmly associated with contagion but it was not till 1793 that BELL distinguished syphilis from gonorrhoea. The development of cellular pathology and microbiology showed the existence of the activity of microbes, and the doctrine of *contagium animatum* was proved by BASSI

(1773–1856). From this time knowledge of the causes of venereal disease rapidly increased following the discovery of spirochaetes in the lesions by DONNÉ and of *Treponema pallidum* by SCHAUDINN. The isolation and cultivation of microbes brought about rapid increase in our knowledge of disease. The study of immunology led to the discovery of the Wassermann and allied tests, as exemplified by antigen-antibody reactions, in 1906; the application of immunology to prevention and treatment followed.

Treatment of venereal disease advanced rapidly after these discoveries; chemistry especially biochemistry led on to chemotherapy first exemplified by Salvarsan; antibiotics followed [hardly enough credit seems to be given to FLEMING in this respect] and these seem to be able to cure almost all types of venereal disease. Drug resistance now presents a problem and may be caused by spontaneous mutation of organisms; if this is so the concurrent use of two drugs seems better than of one, particularly if they are synergic.

Among the many wise sayings is " All the basic sciences have, in different degrees, influenced all the basic medical sciences, which in turn have influenced all the disciplines of medicine and surgery ", and . . . " the prevention of venereal disease will usually be better served by attention to general medical and social measures than by any reliance on drugs ". The author corrects two common fallacies, (1) that clinical observation is imprecise and unscientific, and (2) that laboratory results possess a mystical property which makes them factual and scientific. Clinical science, laboratory science, specific organisms and antibodies are all considered and these are the matters which should appeal most to the modern venereologist.

The control of venereal disease in the future is made difficult by ignorance of the source of infection, difficulty of cure in the later stages, impossibility of checking illicit sexual intercourse and the high susceptibility of a new host. The key may be in the wider and more nebulous fields of psychology, education and morality rather than in laws, regulations or drugs; we should remember that the mental aspects of venereal disease are at least as important as the physical.

This is a work of outstanding interest and should be read and reread by all venereologists. *T. E. Osmond*

WILLCOX, R. R. **Prostitution and Venereal Disease. Social Considerations of Prostitution.** *Brit. J. Preventive & Social Med.* 1961, Jan., v. 15, No. 1, 42–7. [Numerous refs.]

This article should be of very great interest to public health officers, moral welfare workers, social reformers and many others. Some of the facts elicited will surprise many people. A large number of figures are included all of which cannot be reproduced but the trends are important. Prostitution is only one, and not a very large factor in the spread of venereal disease; the " pick-up no fee " type or the " good-time " girl is probably more responsible.

Itinerant males, especially seamen, constitute the majority of male patients; in the U.K. 37·5% of all infected males were immigrants. On the other hand the female is usually static and lives in her own count Economic and social conditions affect the issue; u employment, poverty and hunger favour prostitution. T law of supply and demand works in this matter; th are far more prostituants—the male partners—th prostitutes; the former have been divided into 5 ca gories, or types: (1) where risk of venereal disease simply an episode, (2) where help is needed in taki responsibility, (3) where real conflict in life needs he (4) people with shallow roots, (5) people existing on fringe of crime. Alcohol is frequently a factor; pros tutes seek their clients among drinkers, and alcohol moves inhibitions; alcohol may encourage prostituti and prostitution may boost the sale of alcohol.

Finally, what may surprise some people, the risk contracting venereal disease from a prostitute is mu lower than is commonly believed; numerous figures support of this are quoted; in one investigation average number of exposures before infection was 1 [Brothels are hardly mentioned; in many countries the have been abolished but it is at least doubtful if this h resulted in any great decrease in venereal disease.]

T. E. Osmond

JUNG, H. D. & SOMMER, R. Zur Epidemiologie u Sozialhygiene der Geschlechtskrankheiten im Bezi Neubrandenburg von 1953–1959 (unter besonde Berücksichtigung der Jahre 1953–1956). [E **demiology and Social Hygiene of Venere Diseases in Neubrandenburg — 1953–195** *Ztschr. f.d.g. Hyg. u. ihre Grenzgebiete.* Berl 1961, Mar., v. 7, No. 3, 187–203, 14 figs. [24 ref

This is a painstaking account of the changes in venere disease incidence in the Neubrandenburg region (once part of Mecklenburg) in the period 1953–1959 with pa ticular reference to 1953–1956. The statistics deriv from official notifications and other sources are compar with those of other regions in the German Democra Republic. The number of new cases of venereal disea ascertained in Neubrandenburg diminished from 2,380 1953 to 780 in 1959. These figures represent an incide per 10,000 of population of 33·9 and 11·83 respective

There is a detailed analysis of this experience by a sex and marital status with an account and discussion social hygienic investigations which were made to d cover the sources of infection.

The age distribution of new cases showed no unexpe ted character but the sex distribution in the period 195 1956 showed a considerable excess of female infectio over male at ages 16–20 and 26–40 years, a differen which is partially explained by the fact that venere infections in soldiers were not included. In discussion the origins of infections it is stated that infection throu " casual acquaintances " was relatively common and al that there was a comparatively high morbidity in t married of both sexes.

The incidence of venereal disease in Neubrandenbu is now less than the average for the German Democra Republic as a whole. This decline is believed to be d in part at any rate, to the welfare work which has be carried out aided by legal measures of control.

M. E. Delafield

VERNIER, M. L'épidémiologie syphilitique chez les détenus nord-africains dans les prisons du département de Seine-et-Oise (années 1955, 1956, 1957, 1958, 1959 et trois premiers trimestres 1960). [**The Epidemiology of Syphilis among North African Prisoners in the Department of Seine-et-Oise in the Years 1955–59 and the Three First Quarters of 1960**] *Bull. Acad. Nat. Méd.* 1961, v. 145, Nos. 9/10/11, 230–34.

The Department concerned has a population of 2,200,000 and contains many factories and workshops in which 9,000 to 14,000 North Africans work; these constitute a floating population. In general they do not tend to conceal disease and are usually quite willing to be examined and treated; moreover they are anxious not to carry disease back when they return to their homes in North Africa. By ordinance all convicted prisoners are compelled to submit to examination; others merely detained rarely raise any objection.

Of 3,272 prisoners examined during the period 1955–1960 3,091 were free from venereal disease; 13 (0·25% [*sic*, but the correct figure appears to be 0·39%]) had primary or secondary syphilis, and 150 (4·58%) late syphilis; total 163 (4·18%). Gonorrhoea and non-gonococcal urethritis and trichomoniasis occurred in much the same way as in the French population; chancroid and lymphogranuloma venereum were rarities.

The incidence of syphilis was found to be, in this period, 1·2% less than in the previous 6 years; the idea that venereal disease is common in the North African population in the Paris region seems to have been wrong.

T. E. Osmond

SORESCO, Maria, STĂNICĂ, Ecaterina & STOIAN, Cecilia. Prepararea serului hemolitic anti-oaie pe cobai si experimentarea lui in reacţia Bordet-Wassermann. [**Preparation of Anti-Sheep Haemolytic Serum in the Guineapig and its Trial in the Bordet-Wassermann Reaction**] *Arch. Roumaines Path. Expér. et Microbiol.* 1961, June, v. 20, No. 2, 295–9. [10 figs.]

The English summary appended to the paper is as follows:—

"The original method of BORDET-WASSERMANN for the serological diagnosis of syphilis has been simplified by using an anti-sheep haemolytic serum prepared in the guinea-pig.

"Since this serum contains both complement and haemolysin, the two titrations (of haemolysin and of complement) are substituted by a single titration of the anti-sheep guinea-pig serum, a suspension of washed sheep cells being used instead of the haemolytic system.

"In order to ascertain the value of anti-sheep haemolytic serum prepared in the guinea-pig as compared to sera prepared in rabbits, parallel Bordet-Wassermann tests were carried out with 302 sera, 82 of which were collected from syphilitic patients in various stages of the disease. Flocculation tests (Citochol and M.K.R. II) were performed at the same time. On the whole, concordant results were obtained.

"A few discordant results appear to point to a slightly higher sensitivity of the reactions performed by means of anti-sheep guinea-pig serum (68·97 per cent as against 60·97 per cent).

"As regards the specificity of the reaction, none of the rest of 240 control sera collected from healthy subjects, from patients suffering from various skin diseases or feverish conditions, and from pregnant women gave a nonspecific positive result."

KENT, J. F. & DEWEERDT, J. B. **Diagnostic Utility of the 40-Hour TPI Test.** *Amer. J. Clin. Path.* 1961, June, v. 35, No. 6, 526–7.

"Extending the incubation period of *Treponema pallidum* immobilization (TPI) tests from 18 to 40 hr. revealed specific treponemal immobilizing antibody in specimens of serum from an additional 14·7 per cent of patients examined in a state-wide diagnostic service; similar findings were obtained in a limited study of specimens of cerebrospinal fluid."

METZGER, M., HARDY, P. H., Jr. & NELL, E. Ellen. **Influence of Lysozyme upon the Treponeme Immobilization Reaction.** *Amer. J. Hyg.* 1961, Mar., v. 73, No. 2, 236–44, 1 fig. [22 refs.]

There is some evidence that *Treponema pallidum* possesses a capsule or slime layer composed of non-antigenic material: it is possible that this accounts for the fact that treponemes when first recovered do not react with antibody but do so only after a certain period; this latter may be due to an enzyme released either from the treponemes or from the host tissue debris in which they are suspended.

First hyaluronidase was added to the treponeme suspension but was found to have little effect in shortening the incubation time; later crystalline egg-white lysozyme was tried and this was found to shorten the period appreciably. Further tests showed that the addition of lysozyme did not adversely affect the TPI reaction and it seems that the use of this substance may shorten the time required for the TPI test so that it can be completed in 1 day whereas previously an incubation period of 18 to 20 hours was necessary.

The manner in which lysozyme acts is discussed in some detail and it seems probable that its action precedes the action of antibody and complement on *Trep. pallidum*.

T. E. Osmond

CHACKO, C. W. & YOGESWARI, L. ***T. pallidum* Agglutination Test for Syphilis.** *Indian J. Med. Res.* 1961, Mar., v. 49, No. 2, 196–213. [13 refs.]

These authors in Madras carried out the *Treponema pallidum* agglutination test (TPA) in parallel with the Wassermann (WR), Kahn and VDRL tests on sera from patients with syphilis, treated and untreated, in various stages and on sera from normal persons and those with various diseases, and also on a few cerebrospinal fluids (CSF). Results are set out in 12 tables most of which are

self explanatory [though it is not usual to speak of the *sensitivity* of a test on non-syphilitic sera]. The article is a long one and only a few of the results can be given in an abstract. The antigen was prepared in the usual way. Spirochaetes in rabbits' testes were extracted by shaking in sodium citrate solution which was lightly centrifuged to remove débris and then heavily centrifuged to deposit the organisms which were then taken up in more citrate diluted to contain 60–70 organisms per dark-field; the final suspension was heated at 65°C. for 2 hours and preserved in 1 in 10,000 merthiolate [thiomercal]. The relative sensitivities of the 4 tests on sera from untreated syphilitic subjects in various stages were TPA 97·7, WR 99, Kahn 98 and VDRL 99·5; the corresponding specificities, on non-syphilitic sera were 100, 81, 98 and 97. In presumably non-syphilitic sera from persons with various diseases the comparable figures were 96·8, 72·7, 92·3 and 92·6. With CSF the TPA test gave results comparable with the other tests.

Tests on absorbed sera appeared to show that the TPA test detects an antibody different from reagin.

T. E. Osmond

WILKINSON, A. E. **Fluorescent Treponemal Antibody Test. A Preliminary Report.** *Brit. J. Venereal Dis.* 1961, Mar., v. 37, No. 1, 59–63. [15 refs.]

This test (FTA) [this *Bulletin*, 1960, v. 35, 993, 994] was carried out by placing a 4 mm. loopful of a treponeme suspension in a 1 cm. circle on a glass slide, drying, fixing it in acetone adding 0·03 ml. of serum [to be tested] diluted 1 in 200 and incubating for 1 hour at 37°C.; the excess serum was then washed off and 0·03 ml. of conjugate [see below] in 2% Tween 80 in buffered saline was added and incubated for 30 minutes at 37°C.; excess of conjugate was washed off, the slides soaked in saline, mounted in glycerin/water (9/1) and examined with a special optical equipment (for this the original should be consulted).

The anti-human-globulin serum was prepared by injecting 5 mgm. human gamma globulin with Freund's adjuvant into rabbits, and giving a second dose without adjuvant 3 months later and bleeding the animals after 10–14 days; the globulin fraction was precipitated with ammonium sulphate and conjugated with fluorescein isothiocyanate.

Tests on 167 sera from presumably non-syphilitic persons with negative TPI and STS reactions were all non-reactive. In cases of early syphilis FTA was rather more reactive than Reiter protein complement-fixation test (RPCF) and STS especially in treated cases; in latent and late syphilis much the same was found. In 144 "problem" sera, most of which had given positive STS, FTA agreed with TPI except in 2 cases where FTA was positive and TPI negative, one of which was probably syphilitic; on the other hand rather a large number of FTA were negative or weakly reactive when TPI were reactive or weakly so.

It is concluded that the FTA antibody differs from reagin and from RPCF antibody but is, at least, clearly related to immobilizing antibody. The test appears to be both specific and sensitive. *T. E. Osmond*

MONTGOMERY, C. H., KNOX, J. M., SCIPLE, G. W. VANDER STOEP, E. M. **Erythromycin in Trea ment of Early Syphilis.** *Arch. Intern. Me* 1961, May, v. 107, No. 5, 732–5.

A short review of the literature shows that erythr mycin is spirochaeticidal and therefore of value in t treatment of syphilis.

These authors treated 148 patients with primary secondary syphilis, found positive by dark-grou illumination, with 6 different schedules of erythromyc stearate or propionate and observed them for periods u to 12 months. All doses were given 4 times a day. 9 gr of the stearate over 3 days gave a cumulative failure ra of 85·7% at 9 months; 10 gm. over 5 days, 44% at months; 10 gm. over 10 days, 25·6% at 12 months; 20 gr over 10 days, 20·6% at 12 months. For erythromyc propionate the figures were, 20 gm. over 10 days, 3·1 at 9 months, and 10 gm. over 10 days, 8·9% at 5 month

It is concluded that the propionate is superior to t stearate and that 20 gm. of either may prove adequate f the treatment of early syphilis.

[It seems unfortunate that primary and secondary cas are not considered separately since secondary syphil usually requires far more treatment than primary; in ar case the figures quoted for 20 gm. of either drug do n suggest a cure rate anywhere near 100%.]

T. E. Osmond

LAIRD, S. M. **Recent Trends in Male Gonorrhoea i Manchester.** *Brit. J. Venereal Dis.* 1961, Ma v. 37, No. 1, 70–73, 1 fig.

The incidence of gonorrhoea in England and Wal has steadily increased since 1955; on the other hand th in the male in Manchester has shown a sustained dow ward trend since the third quarter of 1959 (493 in t 3rd quarter of 1959 and 315, 294, 400 and 420 in the following quarters). As regards peripheral clinics rou Manchester the decline from 1959 to 1960 was ve small, though in one place there was a rise of 33 ascribe to recent West Indian immigrants.

According to Laird the explanation lies in the almo complete disappearance of street prostitutes; these ladi have retired to the public-houses, clubs, cafés and danc halls where contact with them requires a more delibera action on the part of the male; during 1960 the month figures of arrests of prostitutes fell fairly steadily fro 53 to 29. This report is encouraging as showing t effect of the Street Offences Act [and should pro gratifying to the Wolfenden Committee].

T. E. Osmond

HÄRÖ, A. S. & PÄTIÄLÄ, R. **An Epidemiologic Study of Gonorrhoea in Finland from 1953 1958.** *Bull. World Health Organization.* Geneva 1961, v. 24, No. 3, 394–7.

Notification of venereal diseases is fairly well carrie out in Finland so that the figures given are reasonabl correct. Gonorrhoea incidence has remained fairly stead in the period under review and though the male : fema

ratio has varied between 2·5:1 and 4·5:1 the ratio in 1958 was much the same as in 1938.

As regards age, most cases in married persons occurred in the younger age-groups (people marry earlier than formerly) while most cases in the unmarried occurred in the 25–29-year group; the incidence in teenagers does not seem to have changed appreciably.

The disease is rare in rural areas and most infections occur in Helsinki and some of the larger seaports; among seamen half the cases originated in home ports, ship prostitutes caused infection in 72 cases in 1957 compared with 33 in 1953, but street prostitutes have decreased, being replaced by " pick-ups " in restaurants, dance halls, etc.; the cheapest restaurants and those selling alcohol provided the most cases; the rate of infection was highest during the holidays and weekends. Somewhat surprisingly the reaction of the gonococcus to pencillin does not seem to have changed [this *Bulletin*, 1957, v. 32, 1045].

T. E. Osmond

BROWN, W. J. **The Status of Gonorrhoea in the USA and Current Problems in its Control.** *Bull. World Health Organization.* Geneva. 1961, v. 24, No. 3, 386–94, 1 chart. [Refs. in footnotes.]

In 1944 it was authoritatively stated that penicillin widely used might bring about the virtual eradication of venereal diseases; however in 3 years the reported cases of gonorrhoea in U.S.A. rose from 300,000 to 400,000 and by 1958 the estimated number of cases was 600,000–700,000 or even perhaps 1,000,000.

In the early post-war years the recommended total dosage of penicillin was 200,000 units; this was soon increased to 600,000 and in recent years 1,800,000 units have been used; a single dose of 1,200,000 units of benzathine penicillin should protect from reinfection for 28 days and has shown some good results.

Some of the difficulties in controlling gonorrhoea include self-treatment or under-treatment, lack of reporting by private physicians, difficulty of diagnosis (and treatment) in women, the decreasing susceptibility of the gonococcus to penicillin and the lowered morals of teenagers.

To combat some of these, " speed-zone " epidemiology, educational courses for social workers, nurses and doctors and " cluster techniques " in case-finding have been employed.

On the clinical and laboratory side, identification of the gonococcus by fluorescent antibody technique, efforts to discover a sero-diagnostic test similar to the Wassermann reaction and research to discover a good prophylactic technique might help in solving the problem. One encouraging fact is that the gonococcus which in 1940 was 84% suplhonamide-resistant now appears to be 97% susceptible [this *Bulletin*, 1959, v. 34, 822].

T. E. Osmond

ROIRON, V., RASETTI-NICOD, G. & DUREL, P. Étude de la sensibilité actuelle du gonocoque aux principaux antibiotiques. **[Present-Day Sensitivity of the Gonococcus to Antibiotics]** *Ann. Inst. Pasteur.* 1961, Apr., v. 100, No. 4, 445–62, 2 figs. [25 refs.]

For the last 10 years gonorrhoea incidence has remained steady or even increased in most countries, in spite of the use of antibiotics; this is presumably due to the gradual decrease of sensitivity of gonococci. Figures showing the incidence of gonorrhoea in 7 countries from 1946 to 1959 are given in a table. Partial resistance to penicillin was noted in 1956 in Norway and has been reported from several other countries. Resistance to streptomycin was noted as far back as 1952 and is often absolute, that is, increase of dosage has no effect. In a second table are set out results obtained by various authors in testing various strains of gonococci against penicillin; from this it is clear that more and more penicillin is needed to kill gonococci. The present authors tested the sensitivity of 300 strains of gonococci from October 1958 to February 1960; their technique is set out in detail; they used both the dilution and disk methods.

As regards penicillin 50·4% of strains were sensitive to 0·25 unit/ml., 22% to 0·05 U./ml., 16·2% to 0·1 U./ml., and 1% were completely resistant to 1·0 U./ml.; for streptomycin 9·7% were sensitive to 2·5 μgm./ml., 20·2% to 5 μgm./ml., 39% to 10 μgm./ml., 7·6% to 50 μgm./ml. and 22·9% were resistant to 1,000 μgm./ml.: fortunately strains resistant to streptomycin are usually sensitive to penicillin.

Tetracycline and spiramycin seem to have retained their killing powers and, what is really remarkable, sulphonamides, which had become almost useless, have almost recovered theirs; 93·5% of strains are sensitive to 50 μgm./ml. or less. Results of a comparison of the 2 methods employed are too detailed to be included in an abstract.

T. E. Osmond

DUNLOP, E. M. C. **Incidence of Urethral Stricture in the Male after Urethritis.** *Brit. J. Venereal Dis.* 1961, Mar., v. 37, No. 1, 64–9.

Instrumental (sound and urethroscope) examination of the male urethra was carried out on 3 types of patients; those with gonorrhoea, those with non-gonococcal urethritis (NGU) and those with a history of urethritis. Details of patients, clinics at which seen, race, ratio of gonorrhoea to NGU and incidence of stricture from 1951 to 1958 are given in 4 tables.

In gonorrhoea patients stricture was found in 2 out of 113, in NGU in 16 out of 328 and in patients with a history of urethritis in 5 out of 57. Somewhat surprisingly 17 of the 23 strictures found, occurred in patients who had been treated by modern methods, *i.e.*, antibiotics or sulphonamides. Sites of the 23 strictures found included meatal 5, intrameatal 2, shaft 5, bulbar entrance 7, proximal bulb 3 and shaft and pars nuda 1.

Of 280 patients observed for 1–3 months 1 developed urinary infection within 2 weeks after instrumentation and 18 developed urethritis within 7 weeks; at least in some of these latent infection was stimulated, which appears all to the good.

It seems advisable from the above that test of cure of urethral infection should include passage of sounds and urethroscopy.

T. E. Osmond

ROBINSON, S. C. **Observations on Vaginal Trichomoniasis. I. In Pregnancy.** *Canadian Med. Ass. J.* 1961, Apr. 29, v. 84, No. 17, 948–9.

All newly admitted patients to the Dalhousie prenatal clinic at Halifax, Nova Scotia, July 1959 to July 1960 were examined for *Trichomonas vaginalis* (TV) by direct wet smears and cultures for this and other organisms; of 897 patients 429 (47·8%) showed TV; bacterial flora showed nothing significant and was much the same whether TV were present or not; TV were never cultured from a neonatal source and there was no correlation between maternal morbidity and the presence of TV. The vaginal *p*H ranged between 4·5 and 7·5 independently of the presence or absence of TV.

Most of the patients came from the below-average-income group. The authors found that no "favourable" pattern of vaginal flora or acid-base reaction encouraged growth of TV and consider that even the most stubborn cases of trichomoniasis yield to metronidazole.

T. E. Osmond

MORLUNGHI, C. & RICCIARDI, M. L. Osservazioni sulla resistenza di *Trichomonas vaginalis* nell'ambiente esterno. [**The Resistance of *Trichomonas vaginalis* in the Environment**] *Giorn. di Malattie Infettive e Parassit.* 1961, Feb., v. 13, No. 2, 117–24. [20 refs.]

Considering the unlikelihood of sexual intercourse being the only way by which *Trichomonas vaginalis* is transmitted, the authors have reviewed the literature on the survival of the parasite, and undertaken research.

5 strains of *Trichomonas* from culture (Vate's medium—not otherwise described—was used throughout) showed an average survival time of about 24 hours in a Locke type of solution. The investigation was mainly on *Trichomonas* in vaginal secretion. When kept in sterile pipettes, protected against drying, these survived an average of 26–21 hours at 18°C. and 17–10 hours at −3°C. The age and physiological condition of the patient from whom they had been taken did not appear to have any bearing. *Trichomonas* in vaginal secretion at 18°C. survived for some hours in various kinds of water: up to 4 hours in sea water, from a half to 2 hours in river water. They could survive in chlorinated water (1 mgm. of chlorine per litre) up to 2 hours. Detergent commonly used in laundering at a concentration of 2·5% killed in a few minutes.

The criterion adopted to assess survival was multiplication on culture—it is possible that infectivity judged by their power to multiply in the natural habitat could be even greater than this suggests. The authors express the opinion that their findings would support the view that extra-venereal transmission could be much more frequent than is usually thought.

E. Agius

MANSUKHANI, S. H., GADGIL, R. K. & IRANI, S. B. **Laboratory Aid in the Diagnosis of Trichomonal Vaginitis.** *J. Indian Med. Ass.* 1961, May 16, v. 36, No. 10, 447–9.

These authors investigated material from 100 patients suffering from leucorrhoea and attending a gynaecological department of the J.J. Group of Hospitals, Bombay. 45 were positive for *Candida albicans*, 36 for *Trichomonas vaginalis* (TV) and 19 for neither.

Smears and cultures were employed for the identification of *Trichomonas*. For culture, 2 media were used: (1) simplified tryptone (in place of trypticase) serum (STS), and (2) Vf. bouillon. The latter medium contained beef and beef liver digested in HCl and pepsin with glucose added to make 0·5%; this was bottled in 5 ml. amounts and sterilized in steam for half an hour; before use bacteria-free human serum to 10%, penicillin and streptomycin 100,000 U/ml., and 20. mgm/ml. respectively were added. Incubation was at 37°C. and sub-cultures were made. For *Candida* Sabouraud's medium was employed.

Direct microscopical examination and cultures on STS were negative in 7 of the 36 cases; in 29 cases cultures on Vf. medium were positive 2–3 weeks after treatment. It is concluded that cultures are superior to smears and that the consorts of patients should be examined.

T. E. Osmond

GENERAL INFECTIVE DISEASES

The order in this section is:—**General; Hospital and other Cross Infections; Coccal Infections; Bacterial Infections; Virus Infections.**

GENERAL

POPOVIC, B. Problem zoonoza u NR Srbiji. [**The Problem of Zoonosis in Serbia**] *Higijena.* Belgrade. 1960, v. 12, No. 4, 374–87, 4 graphs. English summary.

The author reviews the statistics of the incidence in Serbia during recent years of certain diseases of animals which are transmissible to man.

Between 1945 and 1959 the number of cases of anthrax among animals has fallen from 1,300 in 1946 to 100 in 1959, and the number of human cases from 1,100 to around the same figure. Around 800,000 cattle and 600,000 sheep have been immunized. The number of cases of rabies in dogs and cats has fallen from about 400 in 1946 to less than 20 in 1959, and the number of human cases from nearly 40 to less than 5. Since 1954 500,000 dogs have been immunized. Glanders has been practically eliminated; whereas in 1947, 90 cases occurred in horses and 70 in man, no cases of the disease were reported in 1956, 1958 and 1959. Brucellosis still remains

a problem, and has increased in extent since the war; in 1959 there were about 1,900 cases in cattle and pigs, and about 400 human cases. The incidence of bovine tuberculosis in government herds has fallen from 34·2% in 1947 to 0·8% in 1959, and in private herds from 8·9% in 1946 to 0·4% in 1959. Swine erisypelas is increasing rapidly, and the number of pigs dying of the disease has risen from 702 in 1957 to 3,084 in 1959; 2,000,000 pigs have been immunized. *D. J. Bauer*

McLean, D. M. **Disease in Nature Communicable to Man.** *Canadian Med. Ass. J.* 1961, May 6, v. 84, No. 18, 995–9. [29 refs.]

This paper is concerned with the zoonotic diseases of Canada. It gives a general discription of the clinical appearance of these infections in man and their diagnosis. 4 zoonoses are discussed in more detail.

Nearly 200 cases of tularaemia have been notified. The disease is tick-borne in rabbits and water-borne in true rodents. Human infection results mainly from skinning rabbits, but occasionally it follows drinking or contamination of skin wounds with water. The virulence for man of *Brucella tularensis* from rodents is lower than infection from rabbits.

Q fever has only occasionally been reported but there was an outbreak of 62 cases in an abattoir in Quebec. Infection of two sisters on a farm is described.

Rabies was present at a low level in wild animals and cattle but a great increase, with a peak incidence of over 600 cases in December 1958, occurred in 1958–59. Though the incidence declined in 1959 the proportion of rabid skunks increased from 4% in 1958 to 25% in 1960 while that of the normal reservoir, the fox, varied little. The skunk is now an important natural reservoir host. Rabies following a skunk bite and causing a fatal infection in a child near Toronto is described.

A virus, named Powassan after the district in Ontario where it was isolated, caused a fatal infection on a child with symptoms of an acute viral encephalitis [see this *Bulletin*, 1960, v. 35, 717]. The virus is related to but distinct from Russian spring–summer encephalitis. Antibodies to this virus were found in 6 persons in Northern Ontario, and chipmunks and red squirrels showed antibodies, but not other animals examined. The probable vector is *Ixodes angustus* which bites man and is occasionally found on squirrels, but human infection may result from skinning infected animals. *T. H. Davey*

Daeschner, C. W., Jr. & Yow, E. M. **Status of Sulfonamides in Therapy of Infections.** *Pediatrics.* Springfield, Ill. 1961, June, v. 27, No. 6, 1022–5.

After a short historical note the authors discuss briefly the advantages and disadvantages of sulphonamides compared with antibiotics. The sulphonamides have all the same basic metabolic activity, and the selection of a particular sulphonamide for clinical use depends on its absorption, distribution, conjugation and excretion. 5 sulphonamides in common use are discussed on those lines—sulphadiazine, sulphisoxazole (Gantrisin), triple sulphonamide mixture, sulphamethoxypyridazine (Kynex) and sulphadimethoxine (Madribon). Except in meningococcal infection, sulphonamides are rarely the drugs of choice in serious illnesses, but in milder infections, especially for out-patient use, they should find a place.

A. B. Christie

HOSPITAL AND OTHER CROSS INFECTIONS

Howells, C. H. L. & Jones, H. E. **Two Outbreaks of Neonatal Skin Sepsis caused by *Staphylococcus aureus*, Phage Type 71.** *Arch. Dis. in Childhood.* 1961, Apr., v. 36, No. 186, 214–16. [13 refs.]

Two small outbreaks of skin sepsis among the babies in 2 maternity units are briefly described. In both the dominant staphylococcus was phage type 71. In 1 outbreak 7 babies were affected, in the other 2, one of whom died. There was a single carrier among the staff in the first unit; a ward sister and the mother of the child who died were carriers of type 71 in the second unit.

R. E. O. Williams

Gillespie, W. A., Alder, V. G., Ayliffe, G. A. J., Powell, D. E. B. & Wypkema, W. **Control of Staphylococcal Cross-Infection in Surgical Wards. A Four-and-a-Half-Year Study.** *Lancet.* 1961, June 17, 1299–303, 4 figs. [11 refs.]

This paper reports a continuation of the valuable investigations of Gillespie and his colleagues at Bristol [see this *Bulletin*, 1960, v. 35, 261]. Most of the analyses concern staphylococcal colonization of open or drained post-operative wounds. During control periods more than one-third of all open wounds became infected by *Staph. aureus*, most of them resistant to several antibiotics and falling into phage group III. In patients infected with staphylococci and given antibiotics, 76·5% of the staphylococci were multiple-resistant compared with 54·6% of those from patients not so treated.

It was commonly difficult to recognize the mode of entry of particular strains of staphylococci into the wards, but introductions by patients with infective lesions and occasionally by nasal carriers, were observed. Nasal carriage by nurses rarely seemed to be an important route of spread.

The preventive measures explored included:—nasal prophylaxis with a neomycin-bacitracin or neomycin-chlorhexidine cream; local chemotherapy of open wounds with a neomycin-bacitracin-polymyxin spray or chlorhexidine powder; hexachlorophene disinfection of baths; disinfection of barbers' equipment, crockery, bedclothes (every 10 days or on the patient's discharge); use of hexachlorophene soap by patients and staff and of chlorhexidine hand-cream by the staff; disinfection of urine bottles.

In the first ward examined the introduction of all the precautions was followed by a drop in the proportion of wounds colonized from 40–50% to about 20%. Subsequent omission of the nasal and wound chemoprophylaxis was followed by no more than a slight increase in the proportion of resistant strains colonizing the wounds.

In a 2nd ward nasal and wound prophylaxis alone had little effect, possibly because of a concurrent increase in the number of urological beds, but the addition of bedding disinfection and later hexachlorophene baths and the chlorhexidine hand-cream reduced the incidence of colonization to a very low level.

In the 3rd ward nasal prophylaxis alone had a more substantial effect but this was greatly increased after hexachlorophene baths and bedding disinfection were added.

In a separate controlled trial of the neomycin-bacitracin-polymyxin spray applied to the wounds at each dressing, 61 wounds treated had a *Staph. aureus* acquisition rate of 11·5% compared with 28·7% for 80 control wounds.

The incidence of staphylococcal complications other than wound infection seemed to be reduced in the wards in which wound colonization was controlled. [The proportion of the colonized wounds that showed any clinical signs of infection is not stated.]

The application of the measures described in this paper have been used with success to halt ward epidemics of staphylococcal infection. *R. E. O. Williams*

LIDWELL, O. M. **Sepsis in Surgical Wounds. Multiple Regression Analysis applied to Records of Post-Operative Hospital Sepsis.** *J. Hygiene.* 1961, June, v. 59, No. 2, 259–70, 1 fig.

"The method of multi-regression analysis as applied to data which are classified in a non-metric manner is discussed, and a set of data relating the risk of post-operation sepsis to various factors is analysed in this way.

"Age over 60, male sex, long duration of operation, incision over 6 in. long and the insertion of a drain in the wound are all found to be associated with increased risk of post-operative sepsis. Operations for appendicectomy and those on the gall bladder have a relatively high basic risk of developing sepsis while operations for gastrectomy or those on the thyroid, and probably thoracic operations, have a low basic risk. The substantial differences in the gross risk of post-operative sepsis associated with the operations performed in the different hospitals included in the analysis are shown to be almost entirely accounted for by differences in the operations performed in them".

FORTUNATO, A., DURANTE, M. & TANCREDI, R. Ricerca dei portatori nasali di stafilococchi coagulasi-positivi nel personale di assistenza della R. Casa Santa dell'Annunziata. Studio degli stipiti batterici isolati mediante antibiogramma e tipizzazione fagica. [**A Study of Nasal Carriers of Coagulase Positive Staphylococci among the Staff of the "Real Casa Santa dell'Annunziata". Antibiotic Sensitivity and Phage Typing of the Strains Isolated**] *Nuovi Ann. d'Igiene e Microbiol.* 1960, Nov.–Dec., v. 11, No. 6, 557–74. [51 refs.] English summary (9 lines).

123 persons (doctors, assistants, nuns and wet nurses) were examined by nasal swabbing. 116 carried *Staphylococcus pyogenes* which, grown on Difco mannitol salt agar fermented the sugar. Of these 89 were coagulase positive. 84·2% of the coagulase positive and 7·4% of the negative were haemolytic. Many mutants resistant to antibiotics were present, only 3 strains being sensitive to all. All the findings are given in 8 tables.

The authors believe that the coagulase test and production of haemolysis are the best indication of pathogenicity. [They refer only to α-haemolysis.] The antibiotics which were least active were streptomycin, penicillin, the tetracyclines, and chloramphenicol, while sensitivity to oleandomycin, erythromycin, novobiocin, neomycin and kanamycin was generally good. Compared with past findings there was an increase in strains resistant to chloramphenicol, running parallel to an increase in its use in the institution. No correlation was detected between phage type and antibiotic sensitivity. The most frequent phage types were 80/81, 31, 80, 81, 29/29a, 29a, 29, and 53/54. Type 80/81 was found almost exclusively in personnel in contact with the newborn and babies under 2 months, in a department where small outbreaks of staphylococcal infections occurred. The carriers of type 3c/51 all had to do with a case of furunculosis caused by this type. *E. Agius*

LIVE, I. & NICHOLS, A. C. **The Animal Hospital as a Source of Antibiotic-Resistant Staphylococci.** *J. Infect. Dis.* 1961, Mar.–Apr., v. 108, No. 2, 195–204. [18 refs.]

An epidemic of skin infection due to *Staphylococcus aureus* type 80/81 and the high nasal carriage rate of this organism in senior veterinary students at the University of Pennsylvania, compared with the low rate in more junior students, prompted the authors to investigate the carriage rate of staphylococci in dogs attending the veterinary hospitals. Contact with animals was largely confined to the senior students.

None of the 445 outpatient dogs or 759 hospitalized animals investigated had staphylococcal disease. 4·9% of the outpatient animals were nasal carriers of strains typable with the basic set of phages (total carriage rate of coagulase positive staphylococci is not given), 2 strains were type 80/81 one of which was resistant to penicillin and tetracycline. Strains of this type were isolated from of 457 dogs on day of admission to hospital, from of 388 dogs after 1–7 days in hospital and from 8 of 11 animals which had been in hospital longer. Strains of a type related to type 80/81 also increased with length of stay in hospital but among the other typable cultures there was no difference in type distribution between hospital and outpatient dogs.

Of the non-typable cultures from outpatient dogs 19·5% were resistant to 1 or more antibiotic while 72·2% of the 334 strains from hospital animals were antibiotic resistant.

The authors conclude that an antibiotic-resistant strain of type 80/81 had become established in their veterinary hospital and they produce evidence that other veterinary hospitals may be similarly infected. They suggest that these hospitals may be a source of infection for man and animals. *M. Patricia Jevons*

NICOL, C. G. M. **Neonatal Streptococcal Meningitis in a Maternity Unit.** *Monthly Bull. Ministry of Health & Pub. Health Lab. Service (directed by Med. Res. Council).* 1961, Apr., v. 20, 68–70.

An outbreak of infection due to a Group A streptococcus type 5/27/44 in infants born in a maternity home, is described. 21 of the 48 infants became infected, 7 had meningitis, 6 developed skin lesions and 8 had infections of the umbilicus which was only detected bacteriologically.

A previous epidemic due to a type 12 Group A streptococcus had necessitated extensive investigations and the home was thought to be free of Group A streptococci on March 10th 1960 when a mother with a very heavy cold was admitted. The first baby with a type 5/27/44 infection was noticed on March 14th and was transferred with its mother to an infectious diseases hospital.

Within the next 16 days 7 babies who had been discharged from the home developed fulminating meningitis and 5 died. 5 were admitted to hospital with other lesions. Investigations revealed 8 of the remaining infants had infected umbilical stumps and type 5/27/44 was isolated from 2 contacts. The source of the infection was not established but was thought to be an active disperser.

M. Patricia Jevons

CONSTABLE, F. L. & HOWITT, L. F. **Outbreak of E.C.H.O. Type 9 Infection in a Children's Home.** *Brit. Med. J.* 1961, May 27, 1483–6, 1 chart.

An outbreak of ECHO 9 infection in a children's home in Edinburgh is described. The home contained 27 children and 17 became ill. The first patient was admitted to hospital with aseptic meningitis. The most common presenting symptoms were abdominal pain and frontal headache. Some patients only had fever. ECHO 9 was isolated from 10 of the affected children. 2 adults were affected and yielded virus. No virus was isolated from other adults tested. It was thought that infection may have been spread by roller towels and these were replaced by paper towels.

A. J. Beale

COCCAL INFECTIONS

The order in this section is:—***Staphylococcus, Streptococcus, Neisseria, others.***

ENGEL, S. Kinderpneumonie. [**Pneumonia in Children**] *Deut. med. Woch.* 1961, June 23, v. 86, No. 25, 1216–17, 1225, 1248, 2 figs. (1 on pl.)

The main purpose of this short paper is to point out that old views on the age distribution of pneumonia in children are erroneous although they are still to be found in medical textbooks. In the era before X-ray examination became possible it was the opinion that pneumonia in children was most frequent at school age. The author of the present paper records his own experience on some hundreds of cases of pneumonia in children. A table shows the age distribution of 211 cases of pneumonia in children—at age 1–3 years the number of cases was 66 (31·0%) with gradual reduction with advancing age to 5 cases (2·3%) at 11–13 years.

It is also stated that in children pneumonia takes a favourable course and only 1 death occurred in some hundreds of his cases. Furthermore the pneumonic changes in children are in general much less than in adults and rarely involve a whole lobe. X-ray examination has also shown that minimal pathological changes, not definitely discernible by auscultation or percussion, may be present and so render it possible to make a positive diagnosis of pneumonia in cases of sickness which present the typical fever curve of the disease.

M. E. Delafield

SANFORD, J. P. & BELLI, J. A. **The Occurrence of Azotemia in Pneumococcal Pneumonia.** *Amer. Rev. Respiratory Dis.* 1961, May, v. 83, No. 5, 704–10, 1 fig. [29 refs.]

The authors studied azotaemia in patients suffering from pneumococcal pneumonia and found it present in 21 of 44 patients in whom the diagnosis was confirmed bacteriologically, and in 9 of 24 patients in whom the diagnosis was made on clinical grounds only. The azotaemia is prerenal in type, due probably to the toxic destruction of protein in the acute disease. The azotaemia is not a grave prognostic finding unless it occurs in patients with existing renal disease: in such patients a fatal hyperkalaemia may develop.

A. B. Christie

See also p. 1020, LANCET, **Aetiology of Erythema Nodosum in Children. Study by a Group of Paediatricians.**

(i) LAPEYSSONNIE, L., BONNARDOT, R., LOUIS, J. & LEFEVRE, M. Première note concernant l'activité d'une dose unique de sulfaméthoxypyridazine par la voie intramusculaire dans le traitement de la méningite cérébro-spinale à méningocoques. [**Single-Dose Treatment of Meningococcal Cerebrospinal Meningitis with Sulphamethoxypyridazine Intramuscularly**] *Méd. Trop.* Marseilles. 1961, Mar.–Apr., v. 21, No. 2, 129–33.

(ii) LAPEYSSONNIE, L. À propos de la récente épidémie de méningite cérébro-spinale au Niger. Activités d'une mission médicale française (3 Mars 1961–7 Avril 1961). [**Activities of a French Medical Mission in the Recent Epidemic of Cerebrospinal Meningitis in Niger**] *Méd. Trop.* Marseilles. 1961, Mar.–Apr., v. 21, No. 2, 172–4.

The second of these papers gives a brief preliminary account of the work done by a French medical team during a recent epidemic of cerebrospinal meningitis in Niger; the first gives details of a successful experiment by this team with a one-dose treatment of the disease. 290 cases of cerebrospinal meningitis were diagnosed between 4th and 31st March, 1961, and 2 cases of pneumococcal meningitis. Group A *Neisseria meningitidis* was cultured

from 21 out of 179 cerebrospinal fluid specimens sent to the Pasteur Institute of Paris. Out of 62,161 persons living in the epidemic area 33,819 were given prophylactic sulphonamides by mouth [the dose is not stated] and of these only one subsequently developed meningitis, despite conditions favouring continuation of the epidemic.

Alongside the standard treatment of cerebrospinal meningitis with sulphonamides, with or without the addition of penicillin, a study was made of the therapeutic activity of a recently developed drug, sulphamethoxypyridazine, the excretion of which is so slow that therapeutic concentrations persist in the blood for at least 48 hours after a dose is taken. In field conditions the advantages of a one-dose treatment are immense; injections are more certain, and carry more prestige, than oral administration. 44 confirmed cases of meningococcal meningitis were therefore treated with a single intramuscular injection of a 25% solution of sulphamethoxypyridazine, the dose ranging from 0·5 gm. for infants of under 1 year to 2·5 gm. for adults. The patients were not selected, and 10 of them were in grave condition when treated. 42 were cured, and both of the 2 who died had been admitted after several days' illness and died within 5 hours. The only adjuvant treatment was cortisone, given to 15 of the patients for their first 48 hours.

The authors hope that this very promising experimental treatment will be tried out by others on a larger scale in the field. *B. B. Waddy*

Schmidt, A. W. & Galvão, A. L. A. Alguns aspectos epidemiológicos da meningite meningocócica no Município de São Paulo. [**Some Epidemiological Aspects of Meningococcal Meningitis in the City of Sao Paulo**] *Arquivos de Hig. e. Saúde Pública.* S. Paulo. 1961, Mar., v. 26, No. 87, 15–39, 10 graphs & 5 maps. [28 refs.] English summary.

This is a study of meningococcal infection in the city of São Paulo between 1935 and 1958. Between 1935 and 1944 and again after 1951 the disease was endemic in the city but between 1944 and 1951 it was epidemic. During endemic periods the greatest incidence was in children in the 0–4-year age-group but during the epidemic period the highest incidence was in the 15–19 age-group.

The number of cases per 100,000 population during endemic years varied from 2·09 to 3·79: in the epidemic period it varied from 4·8 to 25. The disease was most common in winter months and in the areas of the city were socio-economic conditions were poorest.

A. B. Christie

BACTERIAL INFECTIONS

The order in this section is:—***General, Corynebacterium, Haemophilus, Enteric bacteria, Brucella, Pasteurella, Bacillus, Anaerobes, Spirochaetes, Others.***

Uttley, K. H. **The Mortality and Epidemiology of Diphtheria since 1857 in the Negro Population of Antigua, British West Indies.** *West Indian Med. J.* 1960, Sept., v. 9, No. 3, 156–63. [27 refs.]

In Antigua records of the causes of death, which the author believes to be reasonably accurate, have been kept for over a century since 1857. He has collected from the registers the data on age, sex and date and place of death from diphtheria and croup in coloured persons, and has embodied these in a remarkable group of tables. During the period the population of the island, rural in character and poverty-stricken, remained relatively stable at some 30,000 to 40,000. The average annual diphtheria mortality per 100,000 fell very rapidly from 21·8 in the decade 1857–66 to 1·1 in the decade 1887–96, and since then only 2 deaths from diphtheria have been registered. This fall to virtual extinction took place while the average annual infant mortality in the same four decades remained almost constant (213 to 255 per 1,000 live births), and while the average annual birth rates and standardized death rates also changed very little.

It would seem that diphtheria in Antigua burned itself out naturally and without any improvement in environmental conditions, density of population per room, size of family, infant mortality, birth rate, and standardized death rate; and this rapid decline occurred half a century before the corresponding but slower decline of the pandemic in Europe that appeared before the middle of the nineteenth century. Still more remarkable is the evidence from these records that over one-third of all the deaths from diphtheria occurred in infants under 3 months, and over half under the age of 1 year. [It is difficult to understand the latter figures. Considering the poor social circumstances that undoubtedly existed, diphtheria infection would probably be widespread, and very young infants would be exposed to it to an extent that was rare in Europe. But by the same token most of the mothers must have been immune, and why in that case were infants under 3 months not protected by maternally transmitted immunity? Diagnosis a century ago would be very insecurely based, and one wonders if perhaps some form of pneumonia, with or without laryngitis, was not at this age mistaken for diphtheria.]

H. Stanley Banks

Cockburn, W. C. **Deaths from Whooping Cough in England and Wales in 1958 and 1959.** *Monthly Bull. Ministry of Health & Pub. Health Lab. Service (directed by Med. Res. Council).* 1961, May, v. 20, 93–8.

The notifications and deaths from whooping cough in England and Wales have been decreasing rapidly in recent years and a special study was made in 1958 and 1959 on each death registered as due to whooping cough. During the two years there were 50 deaths among infants (and 2 among adults, which were not included in the survey). Information regarding these deaths was requested from the medical officer of health of the area where the death occurred. 14 of the 50 deaths were in infants under the age of 3 months, and 19 others were between 3 months and one year and 9 between one and two years. Respiratory diseases were mentioned as being associated with whooping cough in all but 9 of the deaths, broncho-pneumonia was mentioned in 37. In one-third of the deaths a contributory cause was recorded. The source of infection was generally an elder sibling. 42 of those

who died had not been vaccinated against pertussis, 2 had had 1 injection only, 1 had had 2 injections and 4 had had 3 injections. Of the 4 with 3 injections 2 were normal healthy children, one was a mongol and one was suffering from coeliac disease. The families in which deaths from whooping cough occurred were, on the average, larger than in the general population.

Many of the 26 babies dying in the first 6 months of life must have been infected when only a few weeks old and early vaccination would not have protected them. The author suggests that babies should be shielded from infection by the vaccination or revaccination of the children in the family when the mother becomes pregnant. A reinforcing dose at school entry to protect the younger siblings in the family should be considered. Respiratory complications should be treated as soon as they are suspected. *W. J. Martin*

BONDURIANSKII, I. P. **The Epidemiological Efficacy of Immunization against Pertussis with Shortened Intervals between the Inoculations.** *J. Microbiol., Epidemiol. & Immunobiol.* London. 1960, v. 31, No. 5, 791–4. [Translated from Russian.]

An immunization schedule against whooping cough was investigated in which 3 doses of pertussis vaccine, each of 1·0 ml. were given subcutaneously at intervals of 10 days. During the next 15 months the inoculated and control children were observed for symptoms of whooping cough. Among the inoculated children in communities, 3 (1·5%) had whooping cough and for those outside the communities 11 (1·1%) were ill whereas in the control groups 11·1% became infected.

The author is satisfied that the shorter interval between the inoculations gives satisfactory immunity to whooping cough. *F. T. Perkins*

DRYL, L., GORZELAK, E. & PRAZMOWSKI, W. Mleczna epidemia duru brzusznego w Zgierzu i Łodzi w roku 1950. **[A Milk-Borne Epidemic of Typhoid Fever in Zgierz and Lodz in 1950]** *Przegląd Epidemiol.* Warsaw. 1961, v. 15, No. 1, 33–40, 1 fig. English summary (8 lines).

In 1950 an outbreak of typhoid fever occurred in Łódz and Zgierz, Poland. During the first 10 days of September 30–60 patients were admitted to hospital each day, and there were 570 confirmed cases in all, from among 1,026 patients admitted with a diagnosis of typhoid. The incidence for the year in Łódz was 97·1 per 100,000 and in Zgierz 880·1 per 100,000, compared with 31–66 per 100,000 over the 4 preceding years. Of 138 strains isolated in Łódz and 131 isolated in Zgierz 118 (85·5%) and 121 (92·4%) respectively were of phage-type F1, the remainder being accounted for by A, D1, E1, I-IV and untypable strains. In Zgierz 63 cases occurred among 14,397 persons vaccinated in the same year, and 66 among unvaccinated persons, and there was therefore no evidence that vaccination had been effective. Milk was identified as the source of infection, and contamination had occurred from storage in infected containers after pasteurization at an ambient temperature of 20°C. In an investigation of persons concerned in the distribution of milk and their families 3 typhoid carriers were found among about 4,000 persons investigated, 2 of whom were excreting organisms of phage-type F1. There were also 4 carriers of paratyphoid A and 2 of paratyphoid B. *D. J. Bauer*

AUSTRALIA, WESTERN. **Report of the Commissioner of Public Health** [HENZELL, L.] **for the Year 1958. Enteric Fever in connection with Pollution of Sea Water** [KOVACS, N.] (pp. 21–3). 89 pp. 1959. Alex. B. Davies, Govt. Printer.

Salmonella paratyphi B infections from sea bathing in harbours and from beaches are very rare compared with the incidence resulting from consumption of shellfish. A possible explanation is that the infective dose of *Salm. paratyphi B* for man is relatively high. The infective dose of *Salm. typhi*, on the other hand, is low—probably no more than 1–10 bacilli; yet only a few outbreaks of typhoid fever have been connected with bathing in infected sea water. Biological self-purification of the sea is of a high order, but is inhibited in tidal waters; closing of harbours and estuaries so as to eliminate the rise and fall of tides tends to make faecal pathogens disappear.

Chlorination of sewage effluent is an effective method of lowering the coliform index, and proper chlorination can eliminate the public health hazard that may be present in bathing from beaches.

[See below.] *H. Stanley Banks*

AUSTRALIA, WESTERN. **Report of the Commissioner of Public Health** [HENZELL, L.] **for the Year 1958. Typhoid and City Beach** [SNOW, D. J. R.] (pp. 52–4, 1 map). 89 pp. 1959. Alex. B. Davies, Govt. Printer.

In the early part of 1958 an outbreak of 15 cases of typhoid fever occurred in Perth, of which 10 were associated with City Beach, and one was due to a carrier. The causative organisms were of 5 different phage-types, and this strongly suggested a conglomerate source of infection such as polluted sea water.

Examination revealed a number of faults in the disposal of the sewage of the city, including incomplete treatment of the sewage at the main plant, high concentrations of faecal organisms in City Beach sea water during February, and two breaks in the 300 ft. of the outfall pipe. *H. Stanley Banks*

KAYE, D., SHINEFIELD, H. R. & HOOK, E. W. **The Parakeet as a Source of Salmonellosis in Man. Report of a Case.** *New England J. of Med.* 1961, Apr. 27, v. 264, No. 17, 868–9. [10 refs.]

An infant aged 7 months in New York developed a febrile disease with diarrhoea of a dysenteric type which lasted for 5 days and then began to subside, *Salmonella*

typhi-murium was isolated from the stools on the 1st and 5th days. The patient was treated with chloramphenicol for 7 days and became asymptomatic. The stools were negative on the 8th and 16th days, but *Salm. typhi-murium* was isolated again on the 50th day, despite absence of symptoms.

There were no reports of rats and mice in the apartment house where the child lived with his parents. The parents had no history of fever or diarrhoea and their stools were negative, as were various foods used by the patient.

2 parakeets bought 2–3 weeks earlier were apparently healthy but *Salm. typhi-murium* was isolated from all of 6 droppings from one of the birds examined over a period of 3 weeks. The birds were not handled by members of the household and were confined in a cage suspended 5 ft. from the floor. Feathers and droppings sometimes fell to the floor where the infant crawled. Experiments suggested that the faeces of the infected bird contained up to 27 million salmonellae per gm. It was also shown that *Salm. typhi-murium* could be isolated from dried faeces at room temperature for at least 32 days. Salmonellae could not be isolated from air samples taken from the cage, or from bird seed or gravel. At the wholesale concern from which the parakeets had originally been obtained (from multiple sources, so that the origin of the infected bird could not be traced) study of droppings from 45 birds in 15 cages each containing 50 to 200 parakeets showed them all to be free of salmonellae.

It would seem that the infant was infected from parakeet droppings on the floor on which he played. As there are said to be some 15 million parakeets in American homes today, and they are often kept in or near the kitchen, it is of some importance that the incidence of salmonella infections in these birds should be studied. *H. J. O'D. Burke-Gaffney*

HOLZBERGER, P. C. & SCHOENFELD, S. **Industrial Medical Aspects of the Acute Dysentery Syndrome. A Laboratory, Clinical, and Industrial Study of the Acute Dysentery Syndrome among Workers in a Tropical Oil Refinery.** *J. Occup. Med.* Chicago. 1961, May, v. 3, No. 5, 240–43, 1 fig.

The authors provide staff medical attention to the more than 4,500 employees of an oil company in Aruba, Netherlands West Indies. What they term the dysentery syndrome, in which they include not only frank dysentery but also gastro-enteritis, is an important cause of loss of working time. To study the problem they investigated 200 consecutive patients reporting sick with this trouble at the Employee Medical Centre, excluding those who had already had treatment.

Rectal swabs and fresh stool specimens were plated on SS medium, stools were examined microscopically, and all patients were treated with an intensive one-day course of oxytetracycline in 4 doses of 1 gm. Patients were allowed to rest for 2 hours in the Centre after the first dose, to see if symptoms were sufficiently controlled to resume work.

No less than 67 of the 200 patients were allowed to resume work at the end of this period, and the average time lost by the whole group was only 1·1 days. This remarkably short time lost justified the massive dose of oxytetracycline.

Laboratory findings were positive in 39 only: 34 with cultures positive for *Shigella*, 2 positive for *Salmonella*, 2 with *E. histolytica* trophozoites, and 1 with both *E. histolytica* trophozoites and a culture positive for *Sh. flexneri*. There was little clinical difference between these patients and those in whom no aetiology could be proved.

To investigate the shortcomings of culture methods, a further series were investigated with 3 techniques: inoculation of fresh stool on SS medium; inoculation of rectal swab material on SS medium; and inoculation of rectal swab material on desoxycholate citrate medium. The first 50 cases giving positive results on any medium were compared. Stools on SS medium gave 24 positive out of 50; rectal swab material on SS medium gave 29 positive; rectal swab material on desoxycholate citrate medium gave 33 positive. By using the rectal swab inoculation on the two media 45 positives were obtained, and this is suggested as the best routine method. *A. C. E. Cole*

PUBLIC HEALTH. 1961, July, v. 75, No. 5, 259–85. **Human and Animal Brucellosis. Recent Studies and Prospects for its Control. (a) Epidemiology** [SKONE, J. F.], 259–67. [31 refs.] **(b) Brucellosis in Cattle** [MCDIARMID, A.], 268–74. **(c) Endemiology of Brucellosis in Rural Areas** [BOTHWELL, P. W.], 274–85, 5 maps & 1 fig. [33 refs.]

(a) Skone reviews the history of brucellosis and its reported and estimated incidence in England and Wales. Although unpasteurized milk is an important vehicle of infection, veterinarians and farmers are liable to infection and also to skin sensitization, by exposure to infected material. Occasional accidental injection of Strain 19 vaccine has resulted in clinical brucellosis. Skone refers to the results of an epidemiological study carried out in association with Brodigan among a resident island population of nearly 94,000 (BRODIGAN *et al.* 1960—"*Brucellosis—An Island Epidemiological Study*"); 44 probable cases of acute and 1 of chronic brucellosis occurred in the year December 1958 to December 1959 and Heaf tests, with 1,000-fold concentrated brucellin, showed that 12·5% of pupils attending rural schools and 4% of those at urban schools had positive tests. 6·3% of 520 registered dairy herds were found to be infected on one or more occasions. Success of control measures in other countries is reviewed. It is noted that a National Survey of brucellosis in 3,000 milk herds began on 1st October 1960. It is pointed out that there are large number of herds free from brucella infection and that others could be freed by the removal of one or a few animals.

(b) McDiarmid reviews the incidence of brucellosis in cattle. The delay occasioned in diagnosing the infection in an individual cow tends to nullify action which might be taken to remove it from a herd. Culture on selective media now enables *Brucella abortus* to be identified in a few days but guineapig inoculation remains the most

sensitive method of detection. Mammary gland infection, persisting in the absence of signs of disease in cattle, may be responsible for infection of milk. A plea is made for universal calfhood vaccination with Strain 19 and the discouraging of vaccination of adult cattle. Preliminary experiments to test the immunizing value of a killed vaccine from *Br. abortus* 45/20, which does not produce agglutinins, are giving encouraging results.

(c) Bothwell has mapped the endemiology of brucellosis in rural areas in and around Oxfordshire. Localized pockets of infection appear to exist and better dissemination of information as to the local occurrence of human disease, or of incidence in herds, could lead to a reduction in the incidence of infections. It is suggested that a survey of " rheumatic " ailments and arthritis in relation to the possible role of *Br. abortus* in their aetiology would be instructive.

[Brucellosis is a fruitful meeting point for health officers, epidemiologists, clinicians and veterinarians.]

Frederick J. Wright

McWhinney, I. & Prior, A. P. **Latent Brucellosis in Farmers.** *Brit. Med. J.* 1961, July 8, 80–81.

20 apparently healthy farmers, from one district, who were not known to have suffered from brucellosis, were investigated for evidence of past or present infection by brucellae. A brucellin skin test was performed on each and simultaneously blood was taken for sero-agglutination tests, the latter being repeated on specimens obtained between 2 and 4 weeks subsequently. The brucellin test was negative in 9, positive in 11. An agglutination titre of at least 1 in 40 was found in 8 at the first test and in 10 at the second (recorded on sera from 17 only). After the tests, histories came to light which suggested that 2 of the positive brucellin reactors had previously suffered from clinical brucellosis which had passed unrecognized. The authors note the high infection rate (14 out of 20) and rightly deduce that neither agglutination to a titre of 1 in 320 nor a rise in titre after a positive brucellin test necessarily indicates the presence of an active infection. A positive brucellin skin test is accepted as indicating previous sensitization of the skin by brucellae and agglutinins as evidence of previous invasion of the tissues.

[The authors use the word " latent " to include sensitivity produced by past clinical and subclinical infections. The term " latent " should imply something dormant which might become active.]

Frederick J. Wright

Kamel, J., Abdel Ghaffar, S. & Tadros, M. M. **Experimental Investigation of the Incidence of Brucellosis among Cyraenian and Egyptian Goats.** *J. Arab Vet. Med. Ass.* 1960, Oct-Dec., v. 20, No. 4, 281–3.

Agglutination tests were positive in 5·8% of 4,618 Egyptian goats and negative in 2,275 Cyraenian goats.

Dimitriu, Ofelia, Bonciu, C., Cerbu, A. & Vasilesco, T. Recherches sur les éliminateurs urinaires dans la brucellose humaine. **[Investigation on Urinary Eliminators in Human Brucellosis]** *Arch. Roumaines Path. Expér. et Microbiol.* 1961, Mar., v. 20, No. 1, 21–31. [10 refs.]

The authors investigated the excretion of brucella in the urine of patients infected with *Brucella abortus* or *Br. suis* in Rumania by inoculating guineapigs with centrifuged deposits from the urine. The organisms were not recovered from any guineapig but histological changes, thought to be diagnostic of brucellosis, were found in 22% of 96 inoculated animals but were absent in controls. Only 1·9% of the inoculated guineapigs showed evidence of allergy to brucellae and only 2·5% significant serological changes. Excretion of brucellae was deduced by this method to have occurred in 55·7% of patients with a subacute illness, 14·5% in chronic brucellosis and in 8·3% in latent subclinical forms.

It is suggested that this technique might indicate whether brucellosis is likely to be active. The presence of brucellae in human urine would appear to make the person liable to spread the infection to other people or to domestic animals although it appears to have been established that scanty excretion of brucellae will provide a dose inadequate to produce such an infection.

Frederick J. Wright

Huziwara, T., Hyôdô, S. & Watanabe, Y. Traitement par antibiotiques de tularémie expérimentale. Résponse immunologique d'animal traité. **[Antibiotic Treatment of Experimental Tularaemia. Immunological Response of the Treated Animal]** *C.R. Soc. Biol.* 1960, v. 154, No. 11, 2158–60.

Mice were inoculated with *Brucella tularensis*: 2 days later antibiotic treatment was begun, each antibiotic being given by subcutaneous injection at 6–hour intervals for 10 days. Observation was continued for a total of 30 days, when some survivors were re-inoculated, and others were killed in order to make cultures or to detect surviving organisms by inoculating another mouse with a suspension of the spleen. All the antibiotics, except kanamycin in the smallest of the 3 doses used, saved all or almost all, the animals. Streptomycin and oxytetracycline also sterilized the tissues in almost every mouse: the numbers so examined after treatment with other antibiotics were smaller, but it seems that tetracycline, chloramphenicol and erythromycin were less successful in sterilizing the tissues: the figures for leucomycin and kanamycin seem of doubtful significance. All animals re-inoculated with an apparently variable but large dose of culture survived (this experiment was done for all the antibiotics except oxytetracycline): it is concluded that a " strong " immune response occurs in antibiotic-treated animals.

L. P. Garrod

NIKIFOROV, V. N. **The Cutaneous Form of Anthrax and Bacteriaemia.** *J. Microbiol., Epidemiol. & Immunobiol.* London. 1960, v. 31, No. 8, 1532–40, 4 figs. & 1 diagram. [27 refs.] [Translated from Russian.]

Some of the early references to bacteriological work on anthrax are here described with mention that many authorities at that time "considered anthrax to be a purely septicaemic disease". Later research "has shown that the appearance of anthrax bacilli in the blood is observed much more often and at earlier periods in animals and man than was previously thought, and that bacteriaemia does not imply a state of septicaemia". Some authors have come to the conclusion that the "appearance of the agent of anthrax in the blood is generally of no prognostic significance, for it may be found in the blood stream during the first few hours of the disease, irrespective of the site and mode of infection".

The author of this paper has made observations on 8 cases of cutaneous anthrax, described with 3 detailed case reports, in patients who made full recovery. Anthrax bacilli were isolated from the intestinal contents and in 1 instance from the urine of these patients at different periods of the illness.

From these observations it is suggested that "bacteriaemia is not a chance phenomenon but a component part of the pathogenesis of this disease"

M. E. Delafield

PARNAS, J., ZWOLSKI, W., KOSLAK, A. & WOJTKOWSKA-UMINSKA, RÓZA. Leptospirenuntersuchungen bei Hydrobionten der Wasserbiocenose in einem Naturherd der Leptospirose. [**Studies concerning Endemic Leptospirosis in Aquatic Animals living in Hydrobiocenosis**] *Zent. f. Bakt.* I. Abt. Orig. 1961, v. 182, No. 2, 237–43, 1 fig.

The English summary appended to the paper is as follows:—

"Within an endemic Leptospirosis-area, harbouring a high percentage of Leptospirosis-infected small mammals, a number of 189 water-borne Hydrobiontics were examined. (Amphibiae, Mollusca, Insecta, Hirudinea.) 1 specimen of Bombina bombina was found to show a positive serologic reaction (L. autumnalis), positive serologic reactions were found also in 3 specimens of Rana esculenta (L. australis B, L. mitis, et cetera). Efforts to isolate species of Leptospira were futile. The authors agree with the accepted opinion that Hydrobiontics have but little importance in the epizootiology and epidemiology of endemic Leptospirosis."

MAILLOUX, M. & KOLOCHINE-ERBER, Berthe. Les leptospiroses à *L. pomona* et *L. mitis* chez le porc et l'homme en France. [**Infection with *Leptospira pomona* and *L. hyos* in Pigs and Man in France**] *Ergebn. Mikrobiol. Immunitätsf.* 1961, v. 34, 363–86, 3 figs. [Numerous refs.]

This paper contains a useful and well-documented review of the history and distribution of porcine leptospirosis, especially of infections caused by *Leptospira pomona* and *L. hyos*. However, the bulk of the author's contributions to the subject have already been published [but no reference is made to them; see this *Bulletin* 1961, v. 36, 367, 569]. *L. H. Turner*

KAPPELER, R., BARANDUN, S., LÜTHI, H. & WIESMANN, H. Über eine Laboratoriumsinfektion mit *Leptospira ballum*, Orchitis als Komplikation. [**A Laboratory Infection with *Leptospira ballum* with Orchitis as a Complication**] *Schweiz. med. Woch.* 1961, July 8, v. 91, No. 27, 810–12. [14 refs.]

The English summary appended to the paper is as follows:—

"The authors report the first Swiss case of leptospirosis ballum, a laboratory infection. The disease was transmitted by a bite of an infected mouse. The clinical picture was characterized by the usual symptoms of leptospirosis including a mild participation of the kidneys and liver. In the 4th week healing was complicated by an orchitis and prostatitis of short duration. The observation is compared to 8 similar cases from the literature in which orchitis was also a frequent complication. The pathogenesis of orchitis is poorly understood at the present time. To date no instance of meningitis by leptospira ballum has been reported to the author's knowledge."

ANGELILLO, B. & MELLINO, M. Sulla presenza di anticorpi per leptospire in sieri di bovini della Sardegna centro-settentrionale. [**Presence of Leptospira Antibodies in Sera of Cattle of Northern Central Sardinia**] *Igiene Moderna.* 1960, Nov.–Dec., v. 53, Nos. 11/12, 603–8.

The English summary appended to the paper is as follows:—

"A serological survey by Lysis-agglutination for the presence of leptospiral antibodies has been conducted on the bovine population of Northern Central Sardinia. 5·4% of the 699 sera examined were found to contain antibodies. The predominant serotypes were *L.i.h.*, *L. ballum* and *L. australis* A and B, followed by *L. grippotyphosa*, *L. saxkoebing* and *L. bataviae*."

BUŞILĂ, V. T., TOPCIU, V. & POP, O. Cazuri de leptospiroză bovis la om. [***Leptospira bovis* Infection in Man in Rumania**] *Studii si Cercetări Infrac. microbiol., Microbiol. si Parazitol.* 1958, v. 9, No. 4, 481–4. French summary.

VIRUS INFECTIONS

The order in this section is:—***General Psittacosis-Lympho-granuloma group, Pox group, Respiratory group, Reovirus group, Enteric group, Arthropod-borne group, Others.***

CIBA FOUNDATION [WOLSTENHOLME, G. E. W. & CAMERON, Margaret P., Editors]. **Study Group No. 7. Virus Meningo-Encephalitis, in honour of K. Todorovic.** pp. viii + 120, 6 text figs. & 1 fig. on 2 pls. [Numerous refs.] 1961. London: J. & A. Churchill Ltd., 104, Gloucester Place, W.1. [12s. 6d.]

This little book contains the papers and discussions of a meeting in London on September 27th, 1960, on virus meningo-encephalitis. K. TODOROVIC (pp. 2–5), in whose honour the meeting was held, started with a brief review of the clinical presentation and mentioned also the multiple viral aetiology.

The viruses causing meningo-encephalitis were briefly reviewed by A. D. MACRAE (pp. 6–16). In the period June 30th, 1959 to June 30th, 1960 aetiological diagnosis on 426 cases of this syndrome were reported by the Public Health Laboratory Service laboratories as follows: mumps 147, poliomyelitis 123, ECHO 70, Coxsackie 64, lymphocytic meningitis 20 and herpes simplex 2. However, in a six-month period one laboratory achieved an aetiological diagnosis in only 76 out of 330 patients. 66 of these were made by virus isolation and 10 by serology. N. R. GRIST (pp. 17–23) reported results from south-west Scotland. The variations in aetiology from year to year are stressed. ECHO 9 was predominant in 1956, Frater virus [a new ECHO serotype which grows well in thyroid cells, see DUNCAN, this *Bulletin*, 1961, v. 36, 93] in 1959.

O. KAHLMETER (pp. 24–34) described the clinical features of ECHO 4, 6, 9 and 11 outbreaks. He pointed out that only a short time ago these infections would have been ascribed to non-paralytic poliomyelitis. ECHO infection should be suspected if there are outbreaks of abacterial meningitis in the summer without paralysis or febrile illnesses with a rash in children.

W. F. SCHERER (pp. 37–39) described Coxsackie-like lesions caused by 2 arthropod-borne viruses isolated in Japan. Similar lesions have been observed for foot and mouth disease (PLATT, *J. Path. & Bact.*, 1956, v. 72, 299) and poliovirus [SHWARTZMAN and ARONSON, this *Bulletin*, 1955, v. 30, 184].

G. GIUNCHI (pp. 40–45) reviewed the evidence that Coxsackie viruses cause meningitis and meningoencephalitis. The evidence is that strains of both Coxsackie A and B can cause both syndromes. Coxsackie viruses have also been shown to cause Bornholm disease, herpangina, encephalomyocarditis and pericarditis as well as more minor illness.

E. G. BREWIS (pp. 46–55) described 18 cases of polioencephalitis; 8 had lower motor neurone disease but not the other 10. There were no virus studies.

Arbor viruses were discussed by D. SLONIM (pp. 59–67), N. OKER-BLOM (pp. 68–73) and W. F. SCHERER (pp. 74–81). Louping-ill, Kyasanur Forest disease, Omsk haemorrhagic fever and tick-borne encephalitis were discussed by Slonim. All these viruses are closely related though clinical manifestations vary. Scherer described extensive investigations of the ecology of Japanese encephalitis. This is complicated, involving mosquitoes and vertebrates including man. Each year many new susceptibles appear and a new epidemic occurs. Problems of control are discussed—control of the vector mosquito of vertebrate reservoirs or protection of man either by vaccination or screening against mosquitoes. None of these methods is at present satisfactory.

J. BETHLEM (pp. 84–86) discussed inclusion bodies and pointed out that although these occurred in virus infections either as "colonies" of virus or as a cellular response to infection they did not necessarily indicate virus infection.

A. M. G. CAMPBELL (pp. 87–97) discussed post infectious virus encephalitis briefly but devoted the main part of his paper to the Guillain-Barré syndrome suggesting this might be due to a virus of cats or other domestic animals.

J. D. SPILLANE (pp. 98–100) gave an account of 4 cases of Behçet's disease. *A. J. Beale*

MACCALLUM, F. O., MCDONALD, J. R. & MACRAE, A. D. **Psittacine Birds as a Source of Virus Infection for Man in England.** *Monthly Bull. Ministry of Health & Pub. Health Lab. Service (directed by Med. Res. Council).* 1961, June, v. 20, 114–16.

During a period of 2 years from April 1958 the authors examined 101 dead budgerigars not known to be associated with human illness and 24 live budgerigars suspected as being the source of disease in man, and failed to isolate psittacosis from any of them. In the same period they were successful in obtaining this virus from 3 of 28 ill or dead, recently imported, parrots or parakeets received from 24 different sources, and they mention 7 positive findings by other workers during this period similarly in imported psittacine birds. The authors emphasize the importance of the recently imported psittacines as a source of psittacosis virus.

Incidentally they failed to find poliomyelitis virus in 17 paralysed psittacine birds and express the view that this virus is unlikely to be the cause of paralysis in cage birds [this *Bulletin*, 1958, v. 33, 622, *bis.*]. *S. P. Bedson*

KUKOWKA, A. & STEPHAN, H. Über 23 im Jahre 1959 in der Infektionsabteilung des Krankenhauses Greiz (Thüringen) beobachtete Fälle von Ornithose. **[Twenty-Three Cases of Ornithosis Seen in Greiz Hospital, Thüringia, in 1959]** *Ztschr. f. ärztl. Fortbildung.* 1961, May 1, v. 55, No. 9, 584–7, 3 figs.

This paper describes the cases of ornithosis treated in the Greiz Hospital (Thüringia, Germany) in 1959. In 4 of the 27 patients submitted as suffering from this condition, the diagnosis, based on clinical and epidemiological grounds, was thought so doubtful as to be excluded without further ado. In the remaining 23 the clinical features and sources of infection are considered and compared; the majority of these cases appear to have resulted

from the handling and slaughter of domestic fowls and ducks. And the results of the laboratory confirmatory investigations—isolation of the virus from blood and sputum; complement-fixation test—sought with varying success, are mentioned. [There is nothing new in this paper.] *S. P. Bedson*

McLean, D. M., Walker, Selma J., Wyllie, J. C., McQueen, E. Joan & McNaughton, G. A. **Infections of the Central Nervous System with Mumps and Enteroviruses in Toronto, 1960.** *Canadian Med. Ass. J.* 1961, Apr. 29, v. 84, No. 17, 941–4. [17 refs.]

This is a study of 104 patients suffering from lymphocytic meningitis admitted to the Hospital for Sick Children, Toronto, during 1960. 58 were thought to be suffering from mumps meningoencephalitis; in 46 of these the diagnosis was established either by isolating the virus from the cerebrospinal fluid, in 23 out of 45 fluids tested, or by demonstrating a rise of serum antibodies (in 40). Of the 46 proved cases 21 had salivary gland involvement before and 5 after the meningoencephalitis, while 20 had no such involvement. Of the 46 cases not due to mumps virus, 10 were shown to be excreting Coxsackie viruses—2 were type A9, 3 type B2, 1 type B5 and 4 untyped. Of the 36 not shown to be excreting enteroviruses, 17 were tested and showed no serum antibody rise to enterovirus antigen. *A. B. Christie*

Milosevic, M., Diklic, D. & Jeric, S. Meningitis parotidea kod dece lečene u infektivnoj klinici 1951–1958 god. [**Mumps Meningitis in Children treated at the Clinic for Infectious Diseases in the Period from 1951–1958**] *Higijena.* Belgrade. 1960, v. 12, No. 4, 361–5. English summary.

Between 1951 and 1958, 49 children have been admitted to the Infectious Diseases Hospital in Belgrade suffering from mumps meningitis; 4 were aged 4–5 years, 32 were 5–10 and 12 were 10–14 years. 75% were resident in the city of Belgrade. The onset in most cases was acute, with pyrexia to 39°C., headache and vomiting. Lumbar puncture was performed on 38 patients; the fluid was clear and under slight pressure, with 100–1,000 cells per cmm. In most patients meningitis appeared concurrently with the enlargement of the parotid glands; in 12 there was a history of mumps 8–12 days before admission, and the diagnosis was confirmed serologically, and in 5 patients admitted with a diagnosis of lymphocytic meningitis parotitis developed 4–7 days after the onset of illness. The course was benign in all cases; the temperature fell to normal after 3–7 days and subjective complaints disappeared. The meningeal signs persisted for an average period of 3 days in patients who had not been subjected to lumbar puncture, but for an average period of 8·5 days in the remainder, and the authors therefore advise against carrying out lumbar puncture when the diagnosis is evident. *D. J. Bauer*

Kocen, R. S. & Critchley, E. **Mumps Epididymo Orchitis and its Treatment with Cortisone. Re port of a Controlled Trial.** *Brit. Med. J.* 196 July 1, 20–24, 2 figs. [17 refs.]

The authors treated 18 patients suffering from mump orchitis with analgesics and a course of cortisone startin with 300 mgm. for 1 day and totalling 950 mgm. in days. A similar group of 16 patients were treated wit analgesics only. Temperature fell more quickly in th cortisone group but no difference was noted in the dura tion of swelling and pain. Subsequent testicular degene ation was not affected by cortisone and appeared to b related to the duration of the swelling. *A. B. Christie*

Smorodintsev, A. A. & Kliachko, N. S. Imunizare activă împotriva oreionului cu o singură injecţi intradermică de vaccin viu. [**Active Immuniza tion against Mumps with a Single Intraderma Injection of Live Virus**] *Studii şi Cercetări Infrc microbiol., Microbiol. si Parazitol.* 1958, v. 9, Nc 4, 401–11, 6 figs. French summary.

The authors describe the preparation and use of th live mumps virus vaccine developed by them and thei collaborators in the U.S.S.R. Pooled amniotic and allan toic fluids containing the virus are dialysed against buffe and to each litre is added 100 cc. of a stabilizing solutio containing 5 gm. of gelatin and 100 gm. of sucrose pe 100 cc., with penicillin and streptomycin. The liv vaccine thus obtained was freeze-dried or stored at 4°C in the liquid state. It is administered intradermally in dose of 0·1 cc. or subcutaneously in a dose of 0·5 cc., an can be mixed with Salk-type poliomyelitis vaccine im mediately before use. Among 99 children aged 4-13 year vaccinated intradermally a rise in titre of inhibiting anti body was found in 75%, and a 4-fold or greater rise i 58%. At the site of injection a reaction developed con sisting of a zone of erythema 5–30 mm. in diameter whic disappeared after 2–3 days, and which could be used as test of sensitivity to mumps. General reactions were nc observed. The vaccine has been administered to 4,116 c 9,683 Leningrad children aged 3–6 years without a pre vious history of mumps; during the following 18–2 months 30 cases of mumps occurred among the vacci nated children and 423 among the remainder.

D. J. Bauer

Brunyate, W. D. T., Fleming, G. M,. Llopis, A. & Roden, A. T. **The Early Stages of the 195 Influenza Epidemic in England and Wales i relation to the Re-Assembly of School** *Monthly Bull. Ministry of Health & Pub. Healt Lab. Service (directed by Med. Res. Council* 1961, May, v. 20, 88–91.

An attempt is made to correlate the opening of schoo in the autumn of 1957 in 20 towns in Lancashire and th West Riding of Yorkshire with an increase of claims fo sickness benefits in the working population, indicative c the spread of influenza from school to home. It appeare that the reopening of schools was not necessarily

decisive factor; in some areas the epidemic was well established before the schools reopened, in others the reopening may have accelerated the spread of infection.

A. B. Christie

WEAVER, N. K., LIONE, J. G. & MOGABGAB, W. J. **Recurrent Asian Influenza in an Industrial Population.** *Ann. Intern. Med.* 1961, May, v. 54, No. 5, 843–55, 3 figs. [19 refs.]

This is a detailed account of a study of 2 epidemics of acute respiratory disease in an industrial population which was undertaken to obtain clinical, laboratory and epidemiological information on Asian influenza. Observations were also made on the protective effects of immunization which were analysed statistically.

The industrial population consisted of about 6,200 employees at a large oil refinery and petrochemical plant in Baton Rouge, Louisiana. Asian influenza first appeared in September, 1957, with relatively high attack rates above 14 per 1,000 per month continuing with peaks in October (34 per 1,000) and February, 1958 (47 per 1,000). The overall case rate for the whole period was 186 per 1,000. Very few cases occurred in the succeeding months of 1958 and during 1959 but a sharp outbreak occurred in January, 1960, with a peak of 78 cases per 1,000 in February. This recurrence of Asian influenza lasted for about 8 weeks.

The methods adopted in the study are described and include those used for virus isolation and serological determinations. There are also particulars of the influenza vaccines administered at different times, the appraisal of their effectiveness and of the methods of statistical analysis employed.

There is a long discussion. Among the points to which reference is made in the summary are that the antigenically identical strains of Asian virus were isolated in both epidemics and "Vaccination in 1957–1958 and in October, 1959, provided significant levels of protection for inoculated workers during the epidemics. Reduction in cases of clinically recognized influenza in vaccinated employees was 60% in 1957–1958 and 20% in 1960; corresponding reductions in absenteeism were 65% in 1957–1958 and 27% in 1960". In spite of this, however, it is important that "Analysis of the cases of influenza that occurred in 1960 revealed no evidence of immunity due to a previous episode of the disease or to vaccination unless the latter had been administered in the epidemic year".

M. E. Delafield

EICKHOFF, T. C., SHERMAN, Ida L. & SERFLING, R. E. **Observations on Excess Mortality associated with Epidemic Influenza.** *J. Amer. Med. Ass.* 1961, June 3, v. 176, No. 9, 776–82, 4 figs. [21 refs.]

It is well known that during an influenza epidemic the death rate from other causes rises, the chief causes of death affected are respiratory and cardio-vascular diseases, and most of the rise is confined to the older age-groups. The authors estimate that 86,000 excess deaths occurred during 1957–1960 in the United States as a result of 3 epidemics of influenza. An analysis of the data showed that two-thirds of the excess mortality occurred in persons aged 65 and over, and cardiovascular-renal diseases and broncho-pulmonary diseases had the largest excess. The authors conclude that most victims of an influenza outbreak are those who might have lived considerably longer had influenza not claimed them, rather than severely debilitated patients in whom influenza is merely a terminal event. They suggest that immunization with influenza vaccine of the groups with a high risk might be effective in reducing the excess number of deaths during an epidemic of influenza.

W. J. Martin

VERSTEEG, J. Enige beschouwingen over de antistofvorming bij infecties met het influenzavirus-A_2 (A/Azië). [**Some Observations on Antibody Formation in Influenza A_2 (A/Asian) Virus Infections**] *Nederl. Tijdschr. v. Geneesk.* 1961, May 20, v. 105, No. 20, 980–82. English summary.

During the influenza epidemic in Holland in 1957 a survey of the presence of type A2 (A/Asian) haemagglutination-inhibiting and complementing-fixing antibodies was conducted on the serum of 242 coal-miners. 120 of those investigated had respiratory infections and the remainder were symptom-free. In 102 (85%) of the first group type A antibody was demonstrated. Haemagglutination inhibiting antibody was present in the sera of 64 patients (53%) and complement-fixing antibody in 91, (76%). Both types of antibody were present in only 53 (44%) patients. Adenovirus complement-fixing antibody was detected in 29 cases.

Of the sera of 122 healthy persons examined 3 weeks after the height of the epidemic 21 (17%) had antibodies to A2 strain of influenza virus, which indicated an asymptomatic course of the infection in these people.

24 miners were studied serologically from September 1957 to March 1958. Inhibiting antibody declined steadily throughout this time and complement-fixing antibody disappeared. This indicated the weak antigenicity of this strain of influenza virus.

From September 1959 to July 1960, 200 specimens of sera received from the University Hospital, Leyden, were tested for the presence of type A2 antibody. A similar decrease in titre of inhibiting antibody was observed. In July 1960 inhibiting antibody could be demonstrated in 16%, complement-fixing antibody in 6% and both types of antibody in only 3% of all cases studied.

Anne U. Tothill

TARCHILĂ, D., ROTHSCHILD, L., BRONITKI, A., PETRESCU, A. & CÎRNARU, S. Izolarea unei tulpini de virus gripal tip D în Bucuresti. [**Isolation of a Strain of Type D Influenza Virus in Bucharest**] *Studii si Cercetări Inframicrobiol., Microbiol. si Parazitol.* 1958, v. 9, No. 2, 187–91, 1 folding chart. French summary.

Two fatal cases of a febrile illness with cardiac insufficiency, pneumonia and convulsions occurred in 1957 in children aged 6 and 7 years living in the Bucharest area. By the intranasal inoculation of mice with a suspension of lung tissue from both patients strains of virus could

be isolated and passaged in mice and fertile eggs. The strains were identified as type D by haemagglutination-inhibition tests with reference antisera. *D. J. Bauer*

Smorodintsev, A. A., Chalkina, O. M., Burov, S. A. & Ilyin, N. A. **Evaluation of the Epidemiological Effectiveness of Live Influenza Vaccine during the Type A_2 and B Epidemics of 1959.** *J. Hyg., Epidemiol., Microbiol. & Immunol.* Prague. 1961, v. 5, No. 1, 60–68, 2 figs.

A trial of live influenza vaccine was carried out during 1959 on 5 groups of young men aged 19–20 years, the groups varied in size from 1,200 to 2,900. Since the young men had the same conditions of living and working and nutritional standards the comparison has been made between groups. 2 groups had a A_2 vaccine, 2 groups had a polyvalent B vaccine and 1 was an unvaccinated control group. Each group was housed separately and 2 of the groups were completely isolated from the other 3 and when evaluating the results they were considered as 2 experiments. Vaccination was carried out by spraying 0·25 ml. vaccine into each nostril. Fortunately for the purposes of the experiment type A_2 and type B influenza appeared in separate waves during the early part of the year. Men who developed an acute influenzal respiratory infection were compulsorily sent to the local hospital and virological and serological studies were made.

During the first wave of influenza when A2 was prevalent the groups who were vaccinated with A2 had about one-half of the morbidity of the B or control group. During the second wave when the virus was type B the A2 group and the controls had a morbidity about 3 times that of the B group.

In some subjects the virus had not multiplied after vaccination and they apparently had no specific immunity. This was suggested by the large proportion of subjects whose antibody titre did not increase. The authors suggest that a mixture of strains A and B should be used and the vaccine sprayed into the upper respiratory tract 3 times at intervals of 2–3 weeks in the fourth quarter of the year. The additional spraying would, they think, increase the effectiveness of the vaccine by 50%.

W. J. Martin

Quilligan, J. J., Jr., Salgado, P. F. & Alena, Barbara. **Influenza Vaccination in Children.** *Amer. J. Dis. Children.* 1961, May, v. 101, No. 5, 593–601. [38 refs.]

Children in a home for mentally defectives in California were given a monovalent inactivated vaccine containing 400 CCA units per ml. of the A Japan 305 strain of A2 influenza virus followed by further doses of polyvalent vaccine containing strains of other A viruses and one B virus, and the same dosage of the same strain of A2 virus. The first dose was given in October 1957, 6 weeks after most children in the home had had Asian influenza. Some children received 4 doses in all up to August 1959, others, according to the inclination of various paediatricians, were given fewer doses at other times. 88 of the children were given 0·5 ml. of monovalent vaccine and 25% had a febrile reaction; 87 were given 0·1 ml. and only 11% reacted in this way. The mean antibody titres in children receiving 0·5 ml. of vaccine were 2-fold higher than in those receiving 0·1 ml. of vaccine. There was an influenza epidemic in December 1959 and January 1960. 49% of 152 children who had received no vaccine had a febrile respiratory disease but only 13% of 113 children who had received the full 4 doses. The children given less vaccine had more illness: 64 cases in 220 children. There was laboratory evidence of influenza infection in 40% of the illnesses, and of adenovirus in 10% and of herpes simplex in 17%.

D. A. J. Tyrrell

Van Der Veen, J. & Smeur, F. A. A. M. Infecties met para-influenzavirus bij kinderen. **[Infections with Para-Influenza Virus in Children]** *Nederl. Tijdschr. v. Geneesk.* 1961, June 17, v. 105, No. 24, 1181–5. [20 refs.] English summary.

The English summary appended to the paper is as follows:—

"From September 1959 to September 1960 paired sera of 168 children under 10 years of age in hospital with acute respiratory infection were tested for the presence of haemagglutination inhibiting antibodies against para-influenza virus of types 1, 2 and 3. A significant rise in antibody was found in 15 children (9%). 5 patients showed serological evidence of infection with type 1 virus, 1 patient with type 2 and 9 with type 3. Complement-fixation tests for mumps, influenza A and B, adenovirus, psittacosis and Q fever were negative in all cases which were positive for para-influenza virus. All were sporadic cases occurring at any time of the year in children aged from 4 months to 9 years."

Bynoe, M. L., Hobson, D., Horner, J., Kipps, A., Schild, G. C. & Tyrrell, D. A. J. **Inoculation of Human Volunteers with a Strain of Virus isolated from a Common Cold.** *Lancet.* 1961, June 3, 1194–6. [14 refs.]

Volunteers at Salisbury and Sheffield were inoculated with a strain of virus (HGP) isolated from a common cold. Colds were induced most readily (12 out of 32 volunteers) by virus given as nasal drops although almost as readily by applying virus by nasal (2 out of 7) and conjunctival swabs (2 out of 7); no colds were produced when the virus was given by means of throat swabs. Nasal washings, rather than nasal or throat swabs, seemed to be the best way of recovering virus; virus was isolated from 13 of the 16 volunteers who developed colds and from 12 out of 14 volunteers showing antibody rises.

The neutralizing capacity of serum was estimated by measuring the reduction of the ability of the virus to produce microplaques after incubation with the serum at room temperature for 2 hours; the activity of the serum was represented by a constant K which indicated the rate at which serum inactivated virus. Of those volunteers

who were inoculated with virus and developed colds, almost all (14 out of 16) had low levels of antibody ($K<0{\cdot}22$) before inoculation and developed high levels afterwards ($K>3{\cdot}8$). Only 7 of 33 volunteers who did not develop colds had such low antibody levels ($K<0{\cdot}22$); the remainder had higher antibody levels which generally remained unchanged. Thus there was evidence that circulating antibody protected against disease and that vaccination, therefore, might be an effective prophylactic.

D. Taylor-Robinson

WYNN-WILLIAMS, N. **Control of Respiratory Infections in Children by Tetracycline.** *Brit. Med. J.* 1961, Feb. 18, 469–71.

The idea of this investigation was inspired by the work of RITCHIE [this *Bulletin*, 1959, v. 34, 21 *bis*] on the prevention of colds in adults. During the winters of 1958–59 and 1959–60 a controlled trial was undertaken to see if tetracycline in therapeutic dosage for 2 days at the start of an upper respiratory infection in children would prevent the development of bronchitis or a disabling chesty cold. 96 children aged 2–12 years were randomized in 2 groups, one of which received tetracycline and the other a placebo. The drugs were administered at home according to the mothers' judgment and interpretation of the instructions given, the details being entered on a card. The patients were seen at the clinic monthly or interviewed by a health visitor, who collected the cards. Some parents found it difficult to recognize any period of prodromal symptoms long enough for prophylactic treatment, and there were other difficulties interfering with the object of the experiment. Nonetheless bronchitis appeared to be prevented in 58% of upper respiratory infections treated with tetracycline compared with 49% in the control group, and the average durations of time off school per attack were 1·9 and 2·9 days respectively—a slight advantage in the tetracycline group.

H. Stanley Banks

BATESON, P. R. & ALLISON, R. M. **The Treatment of the Common Cold with Antibiotics in a Factory Population.** *Brit. J. Clin. Practice.* 1961, June, v. 15, No. 6, 543–50, 1 folding fig. & 1 graph.

The basic hypothesis is that suppression of the nasopharyngeal bacteria during the short viral phase of a cold (characterized by mucoid or serous nasal secretion only) will prevent the occurrence of severe symptoms characterized by muco-purulent nasal discharge [RITCHIE, this *Bulletin*, 1959, v. 34, 21 *bis*, 22]. The method used here for suppressing the bacteria was to give 1 Soframycin lozenge (Framycetin 10 mgm. and Gramicidin 0·1 μgm.) 6 times daily for 3 days and 1 Soframycin nasal spray (by plastic nebulizer) 3 times daily for the same 3 days, to workers reporting a cold. Nasal and throat swabs, taken from about half the workers participating in the trial and cultured on blood agar plates, showed that the amount of growth before treatment (represented as 100%) was reduced to about 10% of this amount, from both nose and throat, within an hour or two after the first treatment, and that this degree of suppression of bacterial growth was maintained throughout the period of treatment.

47 Soframycin-treated subjects were compared with 41 aspirin-treated subjects. Analysis of the results showed that the Soframycin group tended to improve more rapidly than the aspirin group (78% and 43% improvement respectively) at the end of the second day of treatment—a significant difference. Clinical observation conformed with that of Ritchie, that the earlier the start of treatment in the course of the disease the better the results.

H. Stanley Banks

KAJI, M., KIMURA, M., KAMIYA, S., TATEWAKI, E., TAKAHASHI, T., NAKAJIMA, O., KOGA, T., ISHIDA, S. & MAJIMA, Y. **An Epidemic of Pharyngoconjunctival Fever among School Children in an Elementary School in Fukuoka Prefecture.** *Kyushu J. Med. Sci.* 1961, Feb., v. 12, No. 1, 1–8, 2 figs. [14 refs.]

In an elementary school of 584 school children in the village of Asakura in the Fukuoka Prefecture there occurred an epidemic of 124 cases of fever with upper respiratory involvement and conjunctivitis. The first case was observed on June 24th with only 4 in the succeeding 5 days. In July the incidence rose very rapidly to a peak on the 3rd which was 6 days after a new swimming bath had been used by all the schoolchildren. This bath had been closed after only 1 day of use. The incidence of new cases of fever remained high for some days and then diminished rapidly.

There is an account of the clinical picture of the disease and a table which sets out the percentages of the symptoms and signs in the 124 cases, and their duration. The average length of the febrile period was 4·5 days. Virological and serological examinations carried out on a number of children showed that the epidemic was due to adenovirus type 3. Types 3 and 7 have been shown to be those most frequently responsible for the cases of pharyngoconjunctival fever that have been reported from various countries.

M. E. Delafield

ADAMS, J. M., IMAGAWA, D. T. & ZIKE, K. **Epidemic Bronchiolitis and Pneumonitis related to Respiratory Syncytial Virus.** *J. Amer. Med. Ass.* 1961, June 24, v. 176, No. 12, 1037–9, 1 fig. [10 refs.]

"An epidemic of acute respiratory disease occurring in the first 3 months of 1961, is characterized by mild coryzal symptoms in older individuals and severe symptoms of bronchiolitis, pneumonitis, and occasionally death in infants. The cause of the epidemic appears to be related to the respiratory syncytial (RS) virus which has been isolated in HeLa cell and monkey kidney cell culture preparations. This virus causes a distinctive cytopathic change, the main features of which are a marked syncytium, giant cells, and cytoplasmic inclusion bodies. The epidemic is similar in its epidemiological, clinical, and pathological aspects to an epidemic of pneumonitis in infants characterized by giant cells and cytoplasmic inclusion bodies first reported in 1941."

NUORTEVA, P. **Studies on the Significance of Flies in the Transmission of Poliomyelitis. I. The Occurrence of the Lucilia Species (Dipt., Calliphoridae) in relation to the Occurrence of Poliomyelitis in Finland.** *Ann. Entom. Fennici.* Helsinki. 1959, v. 25, No. 1, 1–24, 13 figs. [38 refs.] **II. The Composition of the Annual Blowfly Population as compared with the Incidence of Poliomyelitis in England during the Years 1949–1952.** *Ibid.*, 25–7, 1. fig. **III. The Composition of the Blowfly Fauna and the Activity of the Flies in relation to the Weather during the Epidemic Season of Poliomyelitis in South Finland.** *Ibid.*, No. 3, 121–36, 6 figs. [22 refs.] **IV. The Composition of the Blowfly Fauna in Different Parts of Finland during the Year 1958.** *Ibid.*, 137–62, 13 figs. [27 refs.]

The idea that poliomyelitis may be transmitted by flies is not new, but most of the investigations have hitherto related to houseflies. The present author recalls the fact that poliovirus has been found in blowflies (especially *Lucilia*) which develop in carrion or in wounds in living animals, and argues that wounds or abrasions may be the portal of entry of virus carried by such flies when attracted to wounds. He draws attention to the prevalence of *Lucilia sericata* at various seasons and in different parts of Finland, and the correlation of these facts with the geographical and seasonal incidence of poliomyelitis. He reports similarly on work done in Britain and the United States.

In the third and fourth papers he discusses in some detail the relationship of this and other blowflies with such climatic features as temperature, cloudiness and wind, and reports on trapping carried out in Finland for the purpose of studying the habits of these flies in 1958. He does not claim that transmission of poliomyelitis by blowflies has been proved, but evidently thinks that there may be something in the idea. He quotes a mass of literature on the flies and their biology.

The papers, which are very full, should be read in detail by those who wish to make themselves familiar with the thesis. *Charles Wilcocks*

VERBEV, P., RANGELOVA, S., GABEV, E. & IVANOV, N. **Poliomyelitis in Bulgaria.** *Acta Med. Scandinavica.* 1961, May, v. 169, No. 5, 611–15, 4 figs.

This paper contains some statistical analysis of the figures of poliomyelitis incidence in Bulgaria from 1926, when the disease was first made notifiable, to 1959 inclusive.

Examination of the total numbers of notified cases during this 34-year period shows that the incidence has increased from 0·25 to 4·55 per 100,000 of population. The disease has occurred throughout the country and has had a considerably greater urban than rural prevalence particularly in epidemic years. Study of the age distribution shows the highest incidence to be in children aged 1–4 years and no shift to the older age-groups has been observed.

The highest seasonal incidence in the epidemic years was in July and was 2 months later in the intervening years.

The case mortality has diminished in the period under study. Follow up of over 1,000 patients revealed residual paralyses in over 50%. *M. E. Delafield*

SABIN, A. B. **Poliomyelitis Incidence in the Soviet Union in 1960.** *J. Amer. Med. Ass.* 1961, Apr. 22, v. 176, No. 3, 231–2, 1 chart.

This is a report prepared by Professor M. P. CHUMAKOV, director of the Moscow Institute for Poliomyelitis Research, with a short preface by Sabin. In this preface Sabin says that the reason revaccination with his strains is being carried out again in 1961 after the successful campaign of 1960 is not because of fears about the adequacy of the first dose but rather "the desire to do even more than may be necessary to achieve complete eradication of poliomyelitis". In 1960 nearly 72¼ million people under the age of 21 received Sabin vaccine in Russia, mainly in candy form. Schedules varied in order of frequency, they were: type 1—type 3—type 2; type 1—trivalent vaccine—trivalent vaccine; type 1—types 1 and 3—trivalent vaccine. Vaccination was well accepted [no rate is given] and there were no complications. A graph shows that the incidence of poliomyelitis was low in all areas where Sabin vaccine was widely used but much higher in areas where Salk vaccine was employed either alone or where it was supplemented later on with attenuated vaccine. Chumakov states that the rate of poliomyelitis incidence was 4 times greater in those unvaccinated than in those who had 3 doses of Salk vaccine, yet insufficient people accepted vaccination to prevent a seasonal rise in incidence. *A. J. Beale*

SASLAW, S. & ANDERSON, G. R. **Aseptic Meningitis and Nonparalytic Poliomyelitis.** *Arch. Intern. Med.* 1961, Apr., v. 107, No. 4, 568–71.

The authors make a plea for the non-committal diagnosis of abacterial meningitis rather than non-paralytic poliomyelitis in cases showing signs of meningeal irritation not of bacterial origin. This diagnosis leads to less alarm among the patient's family and friends and is more accurate since poliovirus, in their experience, is a relatively rare cause of such non-paralytic cases. The results of 19 cases studied in 1958–59 are reported. 11 yielded ECHO 4, 1 ECHO 16 and 2 Coxsackie B2 from the cerebrospinal fluid. 5 patients had no virus in the cerebrospinal fluid but poliovirus (2 type 1, 3 type 3) in the stools. These results are similar to those reported earlier from the same laboratory [SASLAW *et al.*, this *Bulletin*, 1960, v. 35, 587] in 1957–58 except that then other enteroviruses, particularly ECHO 9, predominated. *A. J. Beale*

WALLEY, R. V. **Sensory Loss in Poliomyelitis.** [Memoranda.] *Brit. Med. J.* 1961, July 1, 33.

Type 1 poliovirus was recovered from the faeces and a rise in titre of Type 1 antibody occurred in the sera of

a patient who showed typical motor paralysis and also complete sensory loss up to the level of L2. The author states that of 800 cases of poliomyelitis admitted to Ham Green Hospital, Bristol, in the last 10 years this was the only patient to show sensory changes.

A. B. Christie

ABBASSY, A. S. & ABOULWAFA, M. H. **Evaluation of Transaminase Activity in the Cerebrospinal Fluid in Paralytic Poliomyelitis. Preliminary Report.** *J. Pediatrics.* St. Louis. 1961, July, v. 59, No. 1, 60–67. [19 refs.]

MÜLLER, F. & RICKEN, D. Probleme der Wirkungsprüfung von Poliomyelitis-Impfstoffen. [**Problems of Testing the Efficacy of Poliomyelitis Vaccines**] *Deut. med. Woch.* 1961, Feb. 3, v. 86, No. 5, 199–202. [11 refs.]

The authors have investigated the antigenicity of adsorbed inactivated poliomyelitis vaccine alone and of similar vaccine combined with diphtheria and tetanus toxoids in 17 mostly sero-negative infants aged from 5 to 18 months. Two injections of combined vaccine were given with an interval of 1 month, and 2 further doses of uncombined poliomyelitis vaccine were given 6 and 10 months later. The antigenic response, as determined by serial neutralization tests with dilutions of serum and a constant dose of virus, was inadequate, since only 4 infants developed low titres (4–8) of type I antibody after 2 doses of combined vaccine, and there was no response to types II and III antigen. After the second dose of single vaccine an adequate response had developed in 8 of 11 infants tested. 13 other sero-negative infants aged 4–14 months were given 3 doses of uncombined vaccine with intervals of 1 and 6 months; the antigenicity of the type II component was satisfactory, giving neutralizing titres of 8–128 in all cases after the 3rd injection, but the response to type III was poor (titres of 4–16 in 6 infants only), and there was no response at all to the type I component. The authors conclude that combined poliomyelitis vaccines are not satisfactory and that tests of antigenicity in animals alone do not give reliable information.

D. J. Bauer

PAUL, J. R. **Status of Vaccination against Poliomyelitis, with particular reference to Oral Vaccination.** *New England J. of Med.* 1961, Mar. 30, v. 264, No. 13, 651–8. [51 refs.]

This is an excellent review of the present status of polio-vaccination. Killed poliovaccine, although effective, has not wiped out poliomyelitis mainly because, despite great efforts, too few people have been adequately vaccinated. Some vaccine used in the years 1956–58 was also of suboptimal potency. However, there have been several serious epidemics since killed poliovaccine has been available. Living attenuated vaccine seems to be both safe and almost certainly effective. The marked increase in intestinal resistance suggests that the spread of wild polioviruses during an epidemic might be limited by massive use of the attenuated vaccine. The author thinks it is too optimistic to hope that attenuated vaccines can eradicate virulent polioviruses.

The problems of reversion to virulence and spread to contacts are reviewed. It is noted that both occur and cause theoretical dangers that do not appear to have materialized in practice. It is considered that there are no contra-indications to the use of the vaccine although tonsillectomy, therapy with steroids and acute illnesses are possible contra-indications. The manufacture of living vaccine poses special and difficult problems for the manufacturer and the vaccine may not necessarily be cheaper than the killed variety. It is considered best to give the 3 types of virus separately at intervals of about 6 weeks. Salk vaccination is no bar to the use of living vaccine. Indeed, in this way "double protection" may be afforded. Vaccine is given either in cherry syrup or in candy. The exact method of conducting community-wide living poliovaccine programmes is still a matter for discussion and doubtless the best method will only gradually emerge.

The author believes that oral vaccine will be used on an increasing scale in the coming years in the U.S.A. He also notes that the subject of poliovaccination has been the cause of much controversy and wisely reminds us that the exact method of prevention is only a detail in a campaign which aims to reduce paralytic poliomyelitis to a minimum.

A. J. Beale

DANE, D. S. & DICK, G. W. A., with the technical assistance of E. Moya BRIGGS & R. NELSON. **Antibody to Poliovirus in a Well-Immunised Community.** *Lancet.* 1961, June 3, 1217–19, 5 figs.

The proportion of children with poliovirus neutralizing antibodies in County Down, Northern Ireland was determined in the summer of 1960. There were 250,000 people in the country and 95% of the children over 1 year had been or were completing a course of 3 doses of killed poliovaccine. 73% of the children born on June 1st and December 1st aged 1–15 years gave blood for the investigation. The majority of those not attending had left the county and it was estimated that 90% of the available population was sampled. 97% and 91% had antibodies to types 2 and 3 virus, respectively, in the 1–5-year age-group but only 72% had them to type 1 at a titre of 1 in 10 or greater. More significant, 31 out of 33 tested within 1 year of the 3rd dose had antibodies whereas only 30 out of 47 tested after more than 1 year had them. All but 8 children had antibodies to 2 types of virus and these 8 had them to 1 type. Over the age of 6 years more than 94% had antibodies to the 3 types of poliovirus usually in high titre.

The authors conclude from this study that a fourth dose of poliovaccine should be given to children under 5 years one year after the third dose. They show that there have been 7 cases of poliomyelitis in the years 1958–60 in County Down since vaccination was widely used but recognize that it is too early to reach any conclusions about the effect of the vaccine on the incidence of the disease.

A. J. Beale

Siegert, R. & Enders-Ruckle, G. Zur Beurteilung zentralnervöser "Impfschäden" nach Poliomyelitis-Schutzimpfung mit inaktivierter Vakzine (Salk). **[The Assessment of Central Nervous System Damage after Poliomyelitis Vaccination with Salk Vaccine]** *Deut. med. Woch.* 1961, Feb. 3, v. 86, No. 5, 193–9. [24 refs.]

The authors have carried out serological and virological studies on 8 cases of acute involvement of the central nervous system in children aged from 2 to 13 years which developed shortly after the administration of Salk-type poliomyelitis vaccine. The suspicion of poliomyelitis due to incomplete inactivation of the vaccine could be excluded in 4 cases (ECHO-5 and Coxsackie 3–4 infections, fatal post-operative staphylococcal sepsis and fatal double infection with influenza A2 and herpes viruses). In the remaining 4 children a diagnosis of poliomyelitis was established by the isolation of type I virus in 2 cases and by observations of the neutralizing antibody titre. In 1 child, who developed a transient paresis of the left leg 24 hours after inoculation in the left arm, the infection could not have been derived from the vaccine, but in the remaining 3 the illness developed within 28 days of vaccination, and the possibility of infection from the vaccine could not be excluded.

D. J. Bauer

Knowelden, J., Hale, J. H., Gardner, P. S. & Lee, L. H. **Measurement of the Protective Effect of Attenuated Poliovirus Vaccine.** *Brit. Med. J.* 1961, May 20, 1418–20.

It is impossible to assess the effectiveness of attenuated poliovaccine by means of a controlled trial of the type used for killed poliovaccine. Estimates of effectiveness based upon areas where vaccine has or has not been used or on the trend of morbidity in successive seasons are most unreliable. One of the possible advantages of living vaccine is the rapid onset of alimentary immunity making it effective in the face of an epidemic but such use complicates still more the assessment of the results. In 1958 Hale *et al.* [this *Bulletin*, 1959, v. 34, 991] used attenuated type 2 virus in the face of a type 1 epidemic in Singapore. They found that there were 6 paralytic cases among 200,000 vaccinated as against 179 among 300,000 unvaccinated. These crude figures are subject to bias and impossible to interpret.

A re-analysis has been made of the Singapore data for each week and for each age-group, assuming that age distribution did not vary from week to week. The population was divided into 3 groups—unvaccinated, vaccinated less than 8 days previously and over 8 days previously. Attack rates observed for the unvaccinated were calculated and on this basis the expected numbers of cases in the vaccinated populations were determined and compared with those actually found. The expected number for those vaccinated within 8 days was 10·02 and 8 cases were observed. There were only 5 cases in the group vaccinated more than 8 days previously whereas 39·5 cases would have been expected. This shows a clear protective effect of a type 2 attenuated vaccine in the face of a type 1 epidemic.

[Dick and Dane (this *Bulletin*, 1961, v. 36, Nov.; *Med. Officer*, 1961, v. 106, 44) have criticized this paper mainly because no allowance was made for possible bias introduced by ignoring different areas of Singapore in the analysis. For example they consider that areas experiencing highest attack rates would make the highest demands for vaccine, but these areas are perhaps less likely to experience a continued high incidence of the disease at the end of the epidemic. Knowelden and Hale (*Med. Officer*, 1961, v. 106, 44) rely on the fact that the number of cases in the first 8 days after vaccination (8) was closely similar to the expected number (10) to support the validity of the analysis. There can be no doubt that the type 2 vaccine gave considerable protection against type 1 poliomyelitis in Singapore though the exact level of effectiveness may be open to doubt.]

A. J. Beale

Škovránek, V. **Large Scale Field Trial with Sabin's Live Poliovirus Vaccine in Czechoslovakia.** *Rev. Czechoslovak Med.* Prague. 1960, v. 6, No. 1, 1–14, 2 figs. [12 refs.]

In Czechoslovakia a campaign of vaccinating with 3 intradermal doses of Salk vaccine was considered to have been effective in preventing poliomyelitis. However, in 1958 a campaign with Sabin's attenuated vaccine was instituted. Approximately 100,000 TCD50 of each type of polio vaccine were given (type 1 in December 1958, type 3 in January 1959 and type 2 in February 1959) to children aged 2 to 8 years in the Usti, Liberec, Jihlava and Ostrava regions. It is estimated from small-scale serological studies in these regions that 48,172 children lacking type 1, 23,406 type 2 and 54,856 type 3 antibodies were fed Sabin strains. The response to vaccine in previously negative children aged 2 to 8 years was good: type 1, 34 out of 36, type 2, 13 out of 14 and type 3, 32 out of 34. Unvaccinated children of 2 to 6 years showed a much lower rate of acquisition of antibodies. Thus 8 of 19 for type 1, 6 of 14 for type 2 and 7 out of 21 for type 3 developed antibodies as a result of natural infection. In one region, Plzen, a 4th dose of killed poliovaccine was administered.

The morbidity from poliomyelitis up to August 1959 was 0·65 per 100,000 in the Sabin vaccination areas and 1·19 in the rest of the country. No information is given about the age of the patients, their vaccination status or the security of the diagnosis in either region.

A. J. Beale

Dömök, I., Molnár, Elisabeth & Jancso, Agnes. **Virus Excretion after Mass Vaccination with Attenuated Polioviruses in Hungary.** *Brit. Med. J.* 1961, May 20, 1410–17, 8 figs. [26 refs.]

This most interesting paper records in detail the experiences gained with Sabin's attenuated vaccine in Hungary in 1959 and 1960. In 1959, 2 doses of trivalent vaccine were used in 1 area and in 1960, 3 successive doses of monovalent vaccine were used in another area. The

dose was 10^5 TCD50 [it is assumed that CPD means cytopathic dose] of each type for trivalent vaccine but the dose is not stated for the monovalent vaccine. In the 2 campaigns children under 3 years had high rates of excretion of enteroviruses before vaccination, 32 out of 65 and 50 out of 290, respectively. Poliovirus excretion rates were much higher after the first feeding of trivalent vaccine, 81%, than after re-feeding, 16·2%, demonstrating a degree of intestinal resistance. The excretion rate of type 1 vaccine virus was rare in areas that had had a recent high incidence of poliomyelitis. Although instances of failure to establish vaccine infection in children with prior enterovirus infection were noted, the overall incidence of poliovirus excretion in the first trial was similar in those with or without prior enterovirus excretion.

The effectiveness of the 2 methods of vaccination was compared in the 2 campaigns and for this comparison areas with a similar history of poliomyelitis incidence were selected. The incidence of excretion with the 2 schedules (trivalent and monovalent vaccines respectively) was approximately 35% and 40% for type 1, 60% and 55% for type 2 and 65% and 80% for type 3. Most of the failures to excrete polioviruses were probably due to prior natural infection, an assumption based on a few neutralizing antibody tests made before feeding. During the campaigns, polioviruses isolated from vaccinated people were tested for the reproductive capacity at 40°C. [rct/40] marker. All type 1 and 2 strains remained rct/40 negative but 65 type 3 strains were distributed thus: rct/40 positive 21, doubtful 21 and negative 23.

[This paper is full of information but it is not easy to abstract. In particular, the figures contain so much information that they are more confusing than informative.] *A. J. Beale*

WILLIAMS, W. O. **Bornholm Disease Survey, 1956, 1957 and 1958.** *J. College General Practitioners.* 1961, May, v. 4, No. 31, 181–213, 6 figs. & 1 map. [33 refs.]

In 1956 there was an outbreak of Bornholm disease in Swansea, South Wales. The College of General Practitioners organized a retrospective survey of the incidence of the disease throughout the British Isles in 1956, and obtained further information as to the clinical and laboratory findings by a questionnaire in 1957 and 1958. In all 2,470 cases were reported, of which 2,000 were in in the original Swansea outbreak. In 186 cases the questionnaire was satisfactorily completed, and the author, as recorder, analysed the findings in these, supplementing the information by his own findings in 74 of the original cases which he had attended personally.

The age incidence showed a pronounced peak at 5–15 years, with a secondary peak at 30–35. This appeared to be partly due to children contracting the infection at school and then passing it on to their parents, but there was also a higher attack rate in the children. There was no difference in sex incidence.

The illness was abrupt in onset. Myalgia was universal [as a result of diagnostic definition], and occurred in a costo-diaphragmatic distribution in 86%. Fever occurred in 86%, sweating in 65%, and headache in 63%. Upper respiratory symptoms tended to occur at the beginning (61% of the author's personal series had some oedema of the soft palate), while gastro-intestinal symptoms were later in onset (anorexia 61%, nausea 47%, vomiting 22%). Especially characteristic was a tendency for the pain to shift, and also remission of both the pain and the fever with a relapse after an interval.

While the duration of the illness varied from 1 to 40 days, in 53% it was less than 6 days, and in 96% less than 14 days. The incubation period was from 3 to 7 days, usually 4 to 5 days, while the serial difference between cases varied from 1 to 33 days. This suggests that patients may be infectious from before the clinical onset for a period of 2–4 weeks.

Virus investigations were carried out on 51 patients. In 12 Coxsackie B type 1, and in 14 Coxsackie B type 3 viruses were isolated. There were some differences in the clinical symptoms associated with the different types.

[This is a full and careful account of the disease as seen by the patient and the general practitioner, and particularly for the symptomatology it is advisable to read the original paper.] *A. C. E. Cole*

SURJUS, A. Effets du virus Coxsackie B3 sur la souris gestante et sa transmission transplacentaire. [**Effects of Coxsackie B3 Virus on Pregnant Mice, and its Transplacentary Transmission**] *Ann. Inst. Pasteur.* 1961, June, v. 100, No. 6, 825–7.

The English summary appended to the paper is as follows:—

"Coxsackie virus can be transmitted by the transplacentary route. It may have an influence on fecundation.

"Pregnancy (particularly in the end) sensitizes the mother to the action of the virus; in mice, it inhibits natural and acquired immunity."

BEARCROFT, W. G. C. **The Liver in Infective Hepatitis.** [Correspondence.] *Nature.* 1961, May 6, v. 190, 549–50, 1 fig.

An optical and electron microscope investigation has been carried out on samples of liver obtained by biopsy from 26 African soldiers suffering from infective hepatitis. The biopsies were carried out 5–73 days after the onset of illness. The earliest abnormality observable by light microscopy was enlargement and distortion of the nucleolus with increase in ribonucleoprotein. The nucleus then became swollen and ribonucleoprotein accumulated in the cytoplasm. Electron miscroscope studies carried out on 14 samples showed enlargement of the nucleolus, dilatation of the endoplasmic reticulum and swelling of the mitochondria. The cytoplasm of some cells contained numerous granules 21·5 mμ in diameter, sometimes coalescing in groups of 6–12 to form irregularly spherical bodies 76–103 mμ in diameter. These bodies were seen in 7 livers, being present in 1 case 29 days after the onset of illness, and were not present in 6 liver specimens from healthy persons. The appearance of the bodies is illustrated in a photograph, and it is tentatively concluded that they represent particles of the causative virus.

It is suggested that the progression of liver cell changes in infected hepatitis may parallel that seen in rhesus monkeys infected with yellow fever [*Trop. Dis. Bull.*, 1961, v. 58, 309]. *D. J. Bauer*

SEGAGNI, E., ANSALDI, N. & NIGRO, N. Ricerche sulla reazione di fissazione del complemento nell'epatite contagiosa dell'infanzia. [**Research on the Complement-Fixation Test in Contagious Hepatitis in Infancy**] *Giorn. di Malattie Infettive e Parassit.* 1961, Mar., v. 13, No. 3, 167–9. [10 refs.]

The authors detected a viral entity in the serum of children in the early phase of virus A hepatitis which they considered to be the aetiological agent. This substance was obtained by serial passage in chicken embryo cells in rotating tubes and could be used as antigen in a complement-fixation reaction.

Chicken embryo cells were obtained by cutting up 7-day-old embryos and getting the fragments to adhere to the tube walls by chicken plasma or embryo extract. They were placed in rotating tubes, 0·1 ml. of serum taken from patients in the first week of illness was inoculated per tube. Growth was stimulated by subculturing every 2 days for 4 times. Antigen consists of the culture liquid and cellular fragments from the last passage centrifuged first at 2,000 r.p.m. for 10 minutes, then at 20,000 r.p.m. for 20 minutes. If the antigen is not going to be used at once it is preserved with 0·05% formalin. The antigen was titrated by being put in contact with a mixture of 5 inactivated sera from convalescent cases, both sera and antigen being put up at doubling dilutions from 1/2 to 1/1024. The complement-fixation test was then carried out by the Kolmer-Boerner method. The highest dilution of antigen which allowed the fixation of complement in the presence of the highest dilution of serum was taken as the antigen titre (1 unit of antigen). For the test in actual cases 2 units of antigen were used. This method had to be adopted for lack of immune sera with a known titre. Chicken embryo cell culture fluid either not inoculated or inoculated with normal serum was examined for control purposes.

15 sera were tested, serum being taken in the first and in the sixth to the eighth weeks after onset of hepatitis. There were significant titre increases in 12 cases, increase being 4 times or higher in 2 of them. *E. Agius*

COFFLER, M., VĂTĂȘESCU, A., BALMUȘ, G., MITROIU, O. & LITMAN, S. Valoarea reactiei de hemaglutinare cu eritrocite de *M. rhesus* în depistarea purtatorilor de virus de hepatită epidemică. [**The Value of the Haemagglutination Test with Rhesus Red Cells in the Detection of Carriers of Infective Hepatitis Virus**] *Studii si Cercetări Inframicrobiol., Microbiol. si Parazitol.* 1958, v. 9, No. 4, 447–53. [14 refs.] French summary.

The haemagglutination test with red cells proposed for the diagnosis of infective hepatitis [HOYT and MORRISON, this *Bulletin*, 1957, v. 32, 408] has been carried out on the sera of 666 persons. The result was positive in 48 of 300 (16%) apparently healthy blood donors, with titres of 8–64, in 41% of 212 patients suffering from infective hepatitis and mostly examined between the 3rd and 15th days of illness (titre 8–32), in 25·8% of 89 persons in contact with the disease (titre 8–32), and in 9 of 65 (13·8%) patients with other diseases. These results show that the test is not specific for infective hepatitis, but the authors consider that it might nevertheless have some application, in conjunction with the aldolase test, in the screening of blood donors in order to exclude the possible transmission of serum jaundice. *D. J. Bauer*

BEHRENDS, W. & STEINHARDT, N. Virushepatitis nach Bluttransfusionen. [**Virus Hepatitis after Blood Transfusion**] *Deut. med. Woch.* 1961, Feb. 3, v. 86, No. 5, 207–10, 1 fig. [42 refs.]

In a study of 17,920 blood transfusions carried out over a period of 4 years in the authors' hospital in Erlangen 29 cases of presumed serum hepatitis were detected. The patients concerned had received blood from 17 donors, who were therefore suspected of transmitting the disease, although 312 other patients had received the same blood without developing hepatitis. The suspected donors, who had no history suggesting a previous acute infection of the liver, were investigated by means of liver function tests. The thymol, zinc sulphate, serum transaminase and dehydrogenase tests gave values above the accepted normal levels in 3 donors, and an abnormal value in a single test was also found with 6 other donors. In a parallel investigation of 18 blood donors abnormal values in the liver function tests were also found in 4 persons who had each provided 12–26 transfusions without transmitting hepatitis. *D. J. Bauer*

DE RODANICHE, Enid; JOHNSON, C. M.; GALINDO, P. **St. Louis Encephalitis in Panama. II. Survey of Human Blood for Antibodies against St. Louis and Two Related Group B Viruses, Ilhéus and Yellow Fever** [DE RODANICHE & JOHNSON]. *Amer. J. Trop. Med. & Hyg.* 1961, May, v. 10, No. 3, 387–9. [10 refs.] **III. Investigation of Local Mammals and Birds as Possible Reservoir Hosts** [DE RODANICHE & GALINDO]. *Ibid.*, 390–92. [10 refs.]

II. 195 sera were collected in December 1958 from residents on the Pucro, Paya and Tuira rivers. This is an area of tropical forest where the rainfall is concentrated between May and December. The sera were tested for neutralizing antibody by intracerebral tests in adult mice. The viruses used were St. Louis encephalitis (local strain from *Sabethese chloropterus*) [this *Bulletin*, 1960, v. 35, 166], Ilhéus (Honduras strain from *Psorophora*) [*ibid.*, 1957, v. 32, 216], and yellow fever (French neurotropic). 31% neutralized 1 log or more, 14% 1·5 log or more and 8% 2 log or more of St. Louis virus. 44% neutralized 2 or more log of Ilhéus and 42% neutralized 2 or more log of yellow fever virus. There were 4 single positives against St. Louis, 28 against Ilhéus and 29 against yellow fever. 71 had no antibody against any. A higher proportion of sera from men had antibody than from women. Of the 45 children aged under 10 only

2 had St. Louis antibody and 3 Ilhéus antibody. Yellow fever vaccination had been practised in the area but it is not known how much of the yellow fever antibody detected was from this origin. All 3 viruses are known to be or to have been active in the area.

III. St Louis encephalitis virus was previously shown to occur in the Province of Darién. Sera were obtained from shot and trapped animals in February–April 1959. 139 from mammals, 107 from birds and 2 from reptiles were tested for neutralizing antibody. Of the mammals only 2 *Proechimys semispinosus* had St. Louis antibody and these were also weakly reactive with yellow fever virus. 11 wild birds (3 of 10 herons, 1 of 6 guans, 1 of 8 cormorants, 1 of 10 hawks, 1 of 3 vultures, 3 of 6 toucans and a water turkey) had St. Louis antibody and 6 of them also reacted with Ilhéus virus. Virus isolation was attempted from 48 bird sera: no St. Louis virus was isolated but an unidentified virus was isolated from a hawk (*Helicolestis hamatus*) and a woodpecker (*Dryocopus lineatus*).

[For part I see this *Bulletin*, 1960, v. 35, 166.]

C. E. Gordon Smith

De Rodaniche, Enid & Galindo, P. **Isolation of the Virus of Ilhéus Encephalitis from Mosquitoes captured in Panama.** *Amer. J. Trop. Med. & Hyg.* 1961, May, v. 10, No. 3, 393–4.

Mosquitoes were collected on forested slopes at the junction of the Paya and Tuira rivers and at Cerro Azul 60 km. east of the Canal Zone. A total of 14,406 mosquitoes were inoculated into suckling mice. A pool of 37 *Trichoprosopon* spp. collected at Paya between April and June 1958, and a pool of 89 *Haemagogus spegazzinii falco* collected at Cerro Azul in June 1958 yielded strains of Ilhéus virus. The *Haemagogus* strain made 3 of 7 2-day-old mice sick after 8–9 days and all mice in the next passage in 5 days. Re-isolation was successful. The *Trichoprosopon* strain caused symptoms in 2 of 8 sucklings 10–15 days after inoculation but the 6 survivors were immune to challenge. 10 passages were needed before all inoculated mice were affected. 2nd passage virus had an LD50 of 2·6 log but an ID50 of 6·0 log. 14th passage virus had an LD50 of 5·6 log and an ID50 of 6·5 log. No antigenic difference between the 2 strains could be demonstrated by cross challenge or cross neutralization tests. *C. E. Gordon Smith*

Galindo, P. & De Rodaniche, Enid. **Birds as Hosts of Ilhéus Encephalitis Virus in Panama.** *Amer. J. Trop. Med. & Hyg.* 1961, May, v. 10, No. 3, 395–6.

Birds were obtained by shooting and trapping. 48 sera were obtained in the Province of Darién, and 118 in the Province of Bocas del Toro from more than 40 species. They were inoculated into suckling mice and Ilhéus virus isolated from a little blue heron (*Florida caerulea*) and from a keel-billed toucan (*Rhamphastos sulfuratus*) both collected in March 1960 in lowland swamp in Bocas del Toro. The former strain caused illness in 2 of 7 sucklings after 7 days: after 4 passages all mice were affected. Re-isolation was successful. The latter killed 1 of 7 sucklings after 13 days. Re-isolation was unsuccessful. Both were readily adapted to adult mice. Cross-challenge and cross-neutralization tests showed both to be Ilhéus virus. Sera from 62 birds from Bocas del Toro and 68 from Darién were tested for neutralizing antibody to the Honduras strain of Ilhéus virus. 2 or more log of virus was neutralized by 1 of 5 little blue herons, 1 of 3 snowy egrets (*Leucophoyx thula*), 1 of 3 oropendulas (*Zarhynchus wagleri*), 1 tropical kingbird (*Tyrannus melancholicus*), 1 cacique (*Amblycercus holosericeus*), 1 of 15 chickens and 1 of 4 keel-billed toucans. *C. E. Gordon Smith*

Groot, H., Morales, A. & Vidales, H. **Virus Isolations from Forest Mosquitoes in San Vicente de Chucurí, Colombia.** *Amer. J. Trop. Med. & Hyg.* 1961, May, v. 10, No. 3, 397–402.

Mosquitoes were collected in San Vincente de Chucurí on the forest floor and in the canopy on human bait and with a light trap between November 1958 and March 1960. A total of 41,564 mosquitoes were ground in 748 pools and inoculated into mice. 4 strains of Mayaro virus were isolated from 4 pools of 50 *Psorophora* spp. collected in the valley bottom in November 1958. 5 further strains of Mayaro were isolated from *Psorophora* and 1 from *Aedes serratus* in the last 9 months of 1960. Venezuelan encephalitis virus was isolated from 2 pools of 50 *Psorophora* in November 1958 and 2 strains from *Culex* spp. collected by light trap in May and September 1959. Ilhéus virus was isolated from 3 pools of 48–443 *Psorophora ferox* collected in January and July 1959. Two strains of a virus identical with or closely related to Bussuquara virus were isolated from pools of *Culex* spp. collected in June 1959 and in the last 9 months of 1960. The strains were identified by cross neutralization, cross complement-fixation and cross haemagglutinin-inhibition tests. *C. E. Gordon Smith*

Osterrieth, P. M., Deleplanque-Liégeois, Paula & Renoirte, R. **Arthropod-Borne Viruses in the North-Eastern Part of the Congo. Distribution of Antibodies in Four Rural Communities and Statistical Analysis of the Results.** *Trans. Roy. Soc. Trop. Med. & Hyg.* 1961, May, v. 55, No. 3, 246–57, 1 fig. & 1 map. [27 refs.]

Human sera were collected in 1958–59 from 4 communities in the Congo: from 1 village in the north where there had been an outbreak of yellow fever and Chikungunya [this *Bulletin*, 1960, v. 35, 1252: *Trop. Dis. Bull.*, 1960, v. 57, 1157]—an area of bushy savannah crossed by rivers with forest fringes; and from 3 villages in the rain forest near Basoko. The sera were tested for neutralizing antibody by the method of Smith and Westgarth (*J. Hygiene*, 1957, v. 55, 224) to Semliki Forest (SF), West Nile (WN), dengue-1 (D1), dengue-2 (D2), yellow fever (YF), and Bunyamwera viruses. 16–46% of the communities had SF antibody, 4–26% D1 antibody, 10–46% D2 antibody, 4–30% WN antibody, 16–47% YF antibody and 30–82% Bunyamwera antibody. In a total of 247 sera 42 had only Bunyamwera antibody, 7 only

YF antibody, 4 only D2 antibody and 5 only SF antibody. Significant associations were found in the occurrence of antibody to pairs of group B viruses probably because of the strong serological cross-reactions in this group. There were also significant associations in the occurrence of group B viruses and SF virus where there is no serological relation. This probably indicates ecological association in exposure of the communities to infection. Similar association in individual communities could be demonstrated between YF and Bunyamwera, D2 and Bunyamwera, and SF Bunyamwera viruses none of which pairs are serologically related. It seems probable that YF, D2, Chikungunya (related to SF) and Bunyamwera viruses are active in this area.

C. E. Gordon Smith

WORTH, C. B. & DE MEILLON, B. **Culicine Mosquitoes (Diptera: Culicidae) recorded from the Province of Moçambique (Portuguese East Africa) and their Relationship to Arthropod-Borne Viruses.** *Anais Inst. Med. Trop.* Lisbon. 1960, Jan.–June, v. 17, Nos. 1/2, 231–56. [Numerous refs.]

A review of the literature records 67 culicine species in Portuguese East Africa and recent work brings the total to over 100 species. The records of these species are listed and a broad geographical distribution given for each. Sindbis and Spondweni viruses have been isolated from *Mansonia* (*Mansonioides*) *africana*; Spondweni and Wesselsbron from *M.* (*M.*) *uniformis*; Chikungunya, yellow fever, dengue-1 and dengue-2 from *Aedes* (*Stegomyia*) *aegypti*; and yellow fever from *A.* (*S.*) *simpsoni*. Yellow fever and Zika have been isolated from *A.* (*S.*) *africanus*; Semliki Forest virus from *A.* (*Aedimorphus*) *argenteopunctatus*; Middelburg from *A.* (*A.*) *albocephalus*; and Spondweni from *A.* (*A.*) *cumminsi mediopunctatus*. Middelburg, Spondweni, Wesselsbron, Bunyamwera, AR 136, Pongola, Rift Valley and Sindbis viruses have been isolated from *A.* (*Neomelaniconion*) *circumluteolus*; an unknown Mozambique virus from *A.* (*Skusea*) *pembaensis*. H 336, Germiston and Witwatersrand viruses have been isolated from *Culex* (*Neoculex*) *rubinotus*; and an unknown Mozambique virus from *C.* (*Culex*) *sitiens*. Rift Valley virus has been isolated from *C.* (*C.*) *theileri*; and Sindbis, Wesselsbron and West Nile viruses from *C.* (*C.*) *univittatus*. Chikungunya has been isolated from *C.* (*C.*) *fatigans*; and West Nile from *C.* (*C.*) *antennatus*.

C. E. Gordon Smith

HLOUCAL, L. **Tick-Borne Encephalitis as observed in Czechoslovakia.** *J. Trop. Med. & Hyg.* 1960, Dec., v. 63, No. 12, 293–6.

Although Czechoslovakian tick-borne encephalitis is allied to Russian spring-summer encephalitis and to louping-ill, it varies from these in its clinical picture and also shows some immunological differences. The causal virus, isolated by GALLIA *et al.* [this *Bulletin*, 1949, v. 24, 476], and KREJCÍ in 1949 in Moravia is antigenically more closely related to that of Russian spring-summer encephalitis than to the louping-ill virus. The vector-reservoir is the tick *Ixodes ricinus* which passes the viru trans-ovarially to its larvae, which become infective t small rodents and man. These rodents, which compris the animal reservior, include *Apodemus sylvaticus*, *A flavicollis*, *Clethrionomys glareolus*, *Microtus arvalis Sorex araneus* and *Mus musculus*. The disease in ma has been shown to wax and wane with variations in th rodent population. Serological evidence suggests tha infection may also be transmitted to deer, badgers, foxe and squirrels; goats, though showing no clinical evidenc of the disease, may become infected and may transmi the virus in their milk. It is possible that goat's mil may be an alternative mode of transmission to man.

The disease in man has an incubation period of 7–1 days, with a maximum range of 3–21 days. The illness i often biphasic, in that an initial viraemic phase cause an influenza-like attack of 4–6 days' duration which i followed, after a few days' intermission, by a characteris tic picture of meningo-encephalitis. The last subside rapidly in the course of 6–8 days. Abortive forms, ill nesses in which the 3 classical phases are not clearl defined and a clinical variant in which a meningo encephalitis develops without antecedent symptoms, hav all been encountered. A fatal outcome is exceptional bu convalescence is often protracted, for psychologica symptoms, tremor and paresis may persist for months.

In the viraemic stage the conjunctivae and fauces ar often injected, and occasionally bronchitis, pain over th liver and slight splenomegaly are encountered. The stag of invasion of the central nervous system is marked b headaches, signs of meningeal irritation, tremor of th tongue, jaw and fingers and cranial nerve pareses. Th nerves involved are commonly the third and sixth: rarel the fifth, seventh, ninth and eleventh may be affected Signs of pyramidal tract irritation may be noted but ar usually transient, and spastic paralysis rarely ensues Mid-brain damage causing pupillary and oculomoto signs is often associated with signs of cerebellar dys function and the occurrence of vestibular damage is no infrequent.

A purely meningitic syndrome is also seen and ma be associated with a radiculitis of the cervical segment of the cord. The greatest damage falls on the 5th an 6th cervical nerve roots, the resulting lesion affectin motor function more than sensation. Atrophy of th muscles of the neck and shoulder-girdle results. Signs o transient damage to the pyramidal tracts may usually b observed in the legs at the same time.

The CSF is under increase pressure and shows pleo cytosis of 10–200 cells per cmm.; neutrophils predominat initially but are later replaced by lymphocytes. The pro tein content may be greatly increased. Transient live damage and myocardial changes have also beer demonstrated.

J. H. Walters

WEBB, H. E. & RAO, R. L. **Kyasanur Forest Disease: a General Clinical Study in which some Case with Neurological Complications were observed** *Trans. Roy. Soc. Trop. Med. & Hyg.* 1961, May v. 55, No. 3, 284–98, 3 figs. [20 refs.]

28 consecutive patients with the provisional diagnosi of Kyasanur Forest disease admitted to hospital in th

endemic area in March–April 1959 were studied. Studies of paired sera by haemagglutinin-inhibition, complement-fixation and neutralization tests separated the patients into 3 groups—13 positive diagnoses of Kyasanur Forest disease, 13 not due to Kyasanur Forest disease and 2 doubtful. All the positive patients had been in infected forest and 9 had been bitten by ticks: 6 of the negative patients had been in infected forest and 2 reported tick bites.

Fever and headache, usually not very severe, were the presenting symptoms. 12 of the positive patients had myalgia, usually severe, compared with 7 negative patients in which it was not severe. Cough associated with lung signs was common. Haemorrhagic incidents occurred in 9 positive patients and 5 negative. A patient who gave birth at the height of the disease had no unusual blood loss. 6 of the positive patients had a biphasic illness. The first phase lasted 6–11 days. Bradycardia was common and in one case suggestive of heart block. There was an average fall in blood pressure of about 30 mm./Hg. (diastolic and systolic) in the positive patients compared with about 20 mm. in negative patients. Marked dehydration was common and its correction was the major feature of treatment. Antibiotics were used to combat secondary infections.

The second phase occurred after an afebrile period of 9–21 days and the second fever lasted 2–12 days. There was severe headache and 5 of the 6 had central nervous system abnormalities (neck stiffness, mental disturbance tremor, giddiness, abnormal reflexes). 3 cerebrospinal fluids examined had increased cells, mainly mononuclear, and globulin. Leucopenia was constant in the first phase but mild leucocytosis occurred in the second phase when phagocytosis of erythrocytes, leucocytes and platelets was observed in the peripheral blood. Haematocrit readings were low. 7 of the positive patients had received 1–3 doses of formalinized Russian spring-summer virus vaccine but the disease appeared to be no less severe in those than in the unvaccinated. *C. E. Gordon Smith*

ARMENGAUD, M., FRAMENT, V., BIRAM, D. & MAR, I. D. Les kératites de la rougeole en milieu africain à Dakar. [**Keratitis in Measles Among Africans in Dakar**] *Bull. Soc. Méd. Afrique Noire Langue Française*. Dakar. 1961, v. 6, No. 1, 36–44, 3 figs. [24 refs.]

The authors have studied 32 cases of keratitis among 416 patients with measles in hospital. 18 of these consisted of punctate keratitis coinciding with the eruption and 14 were delayed corneal ulceration. The former is apparently due to the virus; the latter is due to secondary infection and can lead to blindness. The authors felt that they had seen in Dakar corneal complications from measles which had been observed in France at the end of the 19th century. They conclude that measles is an important aetiological factor in corneal damage among young Africans. *D. P. Choyce*

DRĂGĂNESCU, N. Studiu asupra unui germene inframicrobian izolat dintr-un caz de meningită multirecurențială. [**An Infective Agent Isolated from a Patient with Recurrent Meningitis**] *Studii si Cercetări Inframicrobiol., Microbiol. si Parazitol.* 1958, v. 9, No. 4, 439–45, 6 figs. on 2 pls. [11 refs.] French summary.

The author has isolated an infective agent from a patient suffering from multiple attacks of meningitis. The illness began in 1953, and in 1957, during the 6th attack, cerebrospinal fluid was inoculated into rabbits, mice and guineapigs intracerebrally and on the cornea, and also into fertile eggs by various routes. No signs of infection were observed in the animals, thus excluding herpes and certain other common infections, but congestion and thickening were noted on the chorioallantoic membrane, and this effect could be maintained in serial passage. No haemagglutinin could be found in the embryonic fluids. On microscopic examination proliferation involving all layers of the membrane was found, with eosinophil inclusions in the ectodermal cells. In 1958 the patient had another recurrence of meningitis, and the animal and egg inoculations were repeated with identical results. The serum of the patient contained no influenza or Q fever antibodies, but neutralized the agent present in a suspension of infected chorioallantoic membrane. The author draws attention to the MC virus, isolated by MOLLARET and CATEIGNE (*C.R. Acad. Sci.*, Paris, 1952, v. 235, 269) [see also this *Bulletin*, 1953, v. 25, 112] from a patient suffering from a similar illness.

D. J. Bauer

LAURSEN, T., FABER, V. & HANSEN, P. F. **Serum Glutamic-Pyruvic-Transaminase in Infectious Mononucleosis.** *Danish Med. Bull.* 1961, May, v. 8, No. 2, 40–42.

"In material from 40 patients with a definite diagnosis of infectious mononucleosis the serum-glutamic-pyruvic-transaminase value was found to be increased in 90 per cent. This increase was transient and disappeared in most cases in less than three weeks.

"In nine patients with no definite diagnosis of infectious mononucleosis, S-GPT was increased in 33 per cent; in 48 patients with acute tonsillitis, increase was observed in 12 per cent.

"It is concluded that S-GPT determination is a valuable aid in the diagnosis of infectious mononucleosis."

JIM, R. T. S. **Thrombocytopenic Purpura in Cat-Scratch Disease.** *J. Amer. Med. Ass.* 1961, June 24, v. 176, No. 12, 1036–7.

"The association of thrombocytopenic purpura and cat-scratch disease in an 11-year-old boy reported is the third such case in the medical literature. Recovery occurred rapidly and the prognosis was good. Cat-scratch disease should be considered among the infectious diseases that may be complicated by thrombocytopenic purpura."

Bacteriology and Immunity

The order in this section is:—**General; Bacteriostatic and Bactericidal Substances; Bacteria; Rickettsiae; Bacteriophages; Viruses; Immunity.**

Abstracts of papers relating to the bacteriology of plague, cholera, yaws, leprosy and certain other tropical bacterial diseases; of the rickettsial fevers; and of yellow fever, dengue, rabies and certain other tropical virus infections, are published in the TROPICAL DISEASES BULLETIN. *Their titles and page references are cited below in the appropriate sub-divisions of this section.*

GENERAL

STEEL, K. J. **The Oxidase Reaction as a Taxonomic Tool.** *J. General Microbiol.* 1961, June, v. 25, No. 2, 297–306. [41 refs.]

KOVACS'S (*Nature*, 1956, v. 178, 703) method for the oxidase test was applied to 1,660 strains of bacteria belonging to many different genera. The test was recorded as positive when the colour appeared within 10 seconds, and as delayed-positive when it appeared between 10 and 60 seconds. Absence of colour or colour after 60 seconds was recorded as negative.

Gram-negative bacteria can be subdivided usefully by the oxidase test and positive results were obtained consistently with species of the following genera: *Aeromonas, Alcaligenes*; *Lophomonas, Neisseria,* and *Pseudomonas*. The genera *Bordetella* and *Haemophilus* gave variable results. In *Pasteurella, P. haemolytica* and most strains of *P. septica* were positive; *P. pestis* and *P. pseudotuberculosis* were negative. Of the vibrios, only *V. metchnikovii* was negative. Among Gram-positive bacteria the oxidase test did not seem to have the same taxonomic value.

[This reaction is one of the 9 tests by which most of the common medical bacteria can be identified down to genus, as will be shown by the publication of tables worked out in the National Collection of Type Cultures.]

S. T. Cowan

BRENNER, S., JACOB, F. & MESELSON, M. **An Unstable Intermediate carrying Information from Genes to Ribosomes for Protein Synthesis.** *Nature.* 1961, May 13, v. 190, 576–81, 8 figs. [21 refs.]

BARBU, E., PANIJEL, J. & QUASH, G., with the technical collaboration of J. P. DANDEU. Caractérisation immunochimique des ribosomes. [**Immunochemical Characterization of Ribosomes**] *Ann. Inst. Pasteur.* 1961, June, v. 100, No. 6, 725–46, 5 figs. & 1 pl. [12 refs.]

PAGE, R. H.; CALDRONEY, Gladys L.; STULBERG, C. S.; WARFIELD, Melissa A.; ZUELZER, W. W. **Immunofluorescence in Diagnostic Bacteriology. I. Direct Identification of *Hemophilus influenzae* in Smears of Cerebrospinal Fluid Sediments** [PAGE, CALDRONEY & STULBERG]. *Amer. J. Dis. Children.* 1961, Feb., v. 101, No. 2, 155–9, 1 fig. [19 refs.] **II. Identification of Group A Streptococci in Throat Smears** [WARFIELD, PAGE, ZUELZER & STULBERG]. *Ibid.*, 160–63. [13 refs.]

1. Sediments of cerebrospinal fluid were comparatively examined by staining with Gram strain, *Haemophilus influenzae* Type B antibody conjugated with fluorescein isothiocyanate and by cultural methods. Correlation between the 3 procedures occurred in 48 out of 53 specimens tested. In the remaining 5 the presence of fluorescent organisms was correlated with the clinical evidence of *H. influenzae* meningitis and effective antibiotic therapy. In the smears prepared from cerebrospinal fluids which contained organisms other than *H. influenzae* no cross-staining was observed.

II. Two throat swabs were taken from each of 500 patients with acute upper respiratory infections. One was used to make a series of smears, on glass slides, for staining with fluorescein-labelled Group A streptococcal antiserum and also by the Gram method. The fluorescent serum had previously been rendered Group-specific by absorption with Group C streptococci [in contrast see this *Bulletin*, 1961, v. 36, 928]. The second swab was used to investigate the presence of Group A streptococci by cultural methods. Correlation between positive fluorescent staining and isolation of Group A streptococci (in some cases by enrichment culture) was found with 67 specimens. In 29 other cases the presence of fluorescent organisms in the throat swab smears was correlated with clinical evidence of streptococcal infection but Group A streptococci were not isolated. In some patients this may have been due to effective antibiotic therapy, for the authors have previously shown that organisms rendered non-viable by antibiotics retain their serological characteristics. *H. Gooder*

BACTERIOSTATIC AND BACTERICIDAL SUBSTANCES; DISINFECTION

The order in this section is:—**General; Antibiotics; other Therapeutic Substances; Disinfection.**

ROGALSKI, E., MORDARSKI, M., INWAL, Alicja & TKACZOWA, Alicja. Badania nad celowością podawania antybiotyków drogą dooskrzelową. [**Studies on the Advisability of the Intrabronchial Administration of Antibiotics**] *Archiwum. Immunol. i Terapii Dośw.* Warsaw. 1961, v. 9, No. 1, 37–44.

The English summary appended to the paper is as follows:—

"Sixteen patients with suppurative processes of the lungs (bronchiectasis, abscesses) were examined for the behaviour of bacterial flora of the bronchial tree following intrabronchial injections of antibiotics. Before the administration of antibiotics, the bronchial discharge was withdrawn by means of Metras' catheter, the kind of bacteria and their sensitivity to antibiotics being determined. A properly selected antibiotic was given once daily intrabronchially and bacterial flora was checked 5 times, 24 hours after each administration of the antibiotic. It has been found that the intrabronchial administration of antibiotics in chronic suppurative processes of the lungs is a reasonable preparation of the patient for surgical procedure. Intrabronchial route is advisable for antibiotics with wide spectre and the choice of antibiotic should be based on the determination of the sensitivity of a disease conditioning bacterial flora."

LOWBURY, E. J. L., LILLY, H. A., MILLER, R. W. S., CASON, J. S. & JACKSON, D. M. **Treatment of Infected Burns with Methicillin.** *Lancet.* 1961, June 17, 1318–21, 1 fig. [14 refs.]

Penicillin may fail to eliminate haemolytic streptococci from burns because it is inactivated by the penicillinase formed by resistant staphylococci also present in them. Methicillin is not so inactivated, and a trial was therefore made of the treatment of infected burns with intramuscular methicillin in a dose of 1 gm. 6-hourly (an addendum reports equivalent results from 1 gm. 12-hourly, reinforced with oral probenecid). Other patients were given tetracycline 250 mgm. and erythromycin 300 mgm. 6-hourly. Both treatments eliminated haemolytic streptococci from all burns, but methicillin also eliminated staphylococci in 34 of 54 (63%) and tetracycline+erythromycin only from 12 of 47 (25·5%). The efficacy of methicillin in eliminating staphylococci was mainly in burns covered by dressings: in those treated by the exposure method the organisms tended to persist. Of 3,479 strains of staphylococci cultivated from burns during this trial, 3,079 were resistant to penicillin. 2,367 to tetracycline and 2,320 to erythromycin, but none to methicillin, although penicillin-resistant strains were slightly less sensitive to it. Proof was obtained of the resistance of methicillin to staphylococcal penicillinase, and of interference by the latter (in the form of a filtrate of staphylococcus culture) with the action of penicillin but not of methicillin on haemolytic streptococci.

L. P. Garrod

BOYD, E. M. & FULFORD, R. A. **The Acute Oral Toxicity of Benzylpenicillin Potassium in Guinea Pigs.** *Antibiotics & Chemotherapy.* New York. 1961, Apr., v. 11, No. 4, 276–83, 4 figs.

Potassium penicillin G was given in large single doses by stomach tube to guineapigs. Doses of 5 gm. per kgm. or more killed 27 out of 48 animals within 6 hours: the LD50 at 24 hours is stated to be $5{\cdot}36 \pm 0{\cdot}34$ gm. per kgm. Boyd and his colleagues have previously found the lethal dose in this time for rats, mice and rabbits to be very similar: *i.e* the *acute* toxicity for guineapigs differs little from that for other animals. The difference is in the reaction to smaller doses, which are without effect in these other animals but cause death in guineapigs within 3–10 days. The authors describe this effect, as produced by a dose of 2 gm. per kgm. or less, and call it "secondary" as distinct from "primary" toxicity. They report some observations of food and water intake, urine output, body weight, temperature and organ weights and water content, but without throwing any new light on the nature of this condition. They choose to assume that it is "due to a substance produced in lethal amounts several days after the entrance into the body of benzylpenicillin", but offer no evidence of the existence of any such substance. *L. P. Garrod*

HEDGES, A. J. **A Method for estimating Low Concentrations of Diffusible Penicillinase.** *J. Applied Bact.* 1960, Aug., v. 23, No. 2, 269–82, 3 figs. & 1 pl. [27 refs.]

This method depends on the measurement of "exhibition" zones of growth produced by the diffusion of penicillinase from cups in medium containing both penicillin and a sensitive organism. Large assay plates were used, and 3 layers of medium, all containing 0·074 units per ml. of penicillin and the middle also containing $10^6 - 10^7$ staphylococci per ml. 64 cups were cut in each plate, and filled with dilutions of penicillinase (4 being compared in each plate) made in *p*H 7·0 phosphate buffer. The plate was then held at 4°C. for 18 hours to permit diffusion, and incubated at 37°C. for 24 hours. The effect of various factors on the results is discussed, and mathematical analysis is employed to show that the method is capable of a high degree of accuracy in computing the relative potencies even of low-titre penicillinases (*e.g.*, inactivating 2 units penicillin per ml. per hour). It has been used for determining the amounts of penicillinase produced by different strains of staphylococci, and although cultures were sometimes filtered before testing, it is said to make little difference to the results if living organisms are present, unless predifusion is curtailed or the penicillinase concentration is low. [The photograph of an assay plate shows evident bacterial growth in the bottom of some of the cups.]

L. P. Garrod

SĂSĂRMAN, A. & HORODNICEANU, Thea, with the technical collaboration of Rodica CIULLEY. Recherches sur les pénicillinases bactériennes. Note II. Titrage de la pénicillinase par une méthode diffusimétrique directe. [**Investigations on Bacterial Penicillinases. Note II. Titration of Penicillinase by the Direct Diffusimetric Method**] *Arch. Roumaines Path. Expér. et Microbiol.* 1960, Dec., v. 19, No. 4, 563–70, 1 fig. [14 refs.]

This paper gives in a double page table particulars of methods proposed by 11 other authors for titrating penicillinase, and the definition of the unit proposed by them. The further method described here consists of pouring a plate of medium containing a heavy inoculum of the Oxford staphylococcus and 0·1 unit per ml. of penicillin. Cylinders are placed on this to which are added 0·1 ml. of dilutions of the penicillinase to be tested: the plates are kept in the cold for 3 hours and then incubated. A zone of staphylococcal growth is seen round the cylinders, the width of which is determined by the amount of the enzyme present. When the amount is small, growth takes place only in the area enclosed by the cylinder, which has to be removed in order to see it. A unit of penicillinase is proposed which is defined as the amount permitting free growth, in this area only, in a test performed this way. 10 replica titrations of one high-titre penicillinase gave closely concordant results. [This does not mean that tests performed in different laboratories with other media, and various differences in technique such as the depth of the medium, not controlled by the description given here, would be so consistent.] *L. P. Garrod*

DOBRZANSKI, W. T. **Conversion to Streptomycin Resistance (Akiba's Phenomenon) in a Presumably Stationary Population of *Staphylococcus aureus*.** *Antibiotics & Chemotherapy*. New York. 1961, Mar., v. 11, No. 3, 196–204. [12 refs.]

Akiba's experiments consisted of adding streptomycin to washed suspensions of bacteria in a non-nutrient medium: the apparently stationary population became resistant, and he therefore argued that adaptation must have taken place. The present paper is not the first to have pointed out that in fact such a population is not stationary: growth occurs, nutrients being furnished by the lysis of dead cells. The experiments reported here were done with one of the organisms used by Akiba, *Staphylococcus aureus* 209P, and showed the following: (1) This conversion to resistance does not occur unless the inoculum contains a number of cells calculated by determinations of the mutation rate to resistance to contain at least one such mutant. (2) Multiplication up to 1,000-fold took place in Berkefeld filtrates of stored suspensions, or in phosphate buffer containing heat-killed cells. (3) When 10^8 streptomycin-sensitive cells and 10^2 resistant cells which were also resistant to erythromycin, were suspended in buffer containing streptomycin, the streptomycin-resistant population found after some days was also erythromycin-resistant, this proving that it was derived by multiplication from the few resistant cells originally introduced. *L. P. Garrod*

HUGHES, W. H. **The Diminution of Variation in Bacterial Populations with special reference to *Klebsiella pneumoniae* and Drug Resistance.** *J. General Microbiol.* 1961, May, v. 25, No. 1, 157–65, 5 figs. [11 refs.]

Single cell isolation was employed to obtain cultures of a strain of *Klebsiella pneumoniae* sensitive and resistant to streptomycin. These were cultivated separately and together in broth, and from each culture the surface of an agar block containing 10μgm./ml. of streptomycin was inoculated: this was incubated under oil for 3 hours, and the diameter of 100 microcolonies was then measured. Histograms of the results show a peak at a low diameter for the sensitive culture, at a higher one for the resistant, and at an intermediate point for the mixed. Similar results were obtained with chloramphenicol: here there was also a colonial difference between the sensitive culture and the resistant variant, and this difference tended to disappear in mixed culture. When the growth of the 2 was separated by a collodion membrane, their individual characters were retained. "Something analogous to inbreeding" is believed to be the explanation of these findings. *L. P. Garrod*

ZIEGRA, S. R. & STORM, R. R. **Dosage of Chloramphenicol in Premature Infants.** *J. Pediatrics.* St. Louis. 1961, June, v. 58, No. 6, 852–7, 1 fig.

Chloramphenicol in doses of 100 mgm. per kgm. body weight given to premature or full-time infants may cause dangerously high blood levels: the infants may develop abdominal distension, diarrhoea and lethargy and some pass into a state of fatal shock. The authors tried several dosage schemes, assaying blood levels at various intervals. They found that a dose of 25 mgm. per kgm. per day given in divided intramuscular 8-hour doses was insufficient but that given as one intramuscular dose of chloromycetin acid succinate it produced an effective blood level for at least 9 hours for babies under 6 days old. They recommend as a safe and effective dose an intramuscular injection of 25 mgm. chloromycetin acid succinate in one thigh and 25 mgm. of chloromycetin intramuscular (an aqueous suspension of 20 micron chloramphenicol crystals) in the other thigh: these injections will maintain an effective dose in newly born premature infants for 48 hours, when they may be repeated. Premature infants over 4 days old may require this dose every 24 or 36 hours. *A. B. Christie*

MCCURDY, P. R. **Chloramphenicol Bone Marrow Toxicity.** *J. Amer. Med. Ass.* 1961, May 20, v. 176, No. 7, 588–93, 4 figs. [13 refs.]

This paper from the Georgetown University School of Medicine, Washington, D.C., gives the histories of 15 patients, all Negroes, who are alleged to have suffered reversible marrow damage from chloramphenicol. The drug had been given for a variety of indications in doses varying from 28 to 105 mgm./kgm. daily for periods varying from 10 to 71 days. The assessment of damage was based on lowered haematocrit readings (haemoglobin estimations and red cell counts are not

given), and confirmed by finding a lowered (or *nil*) reticulocyte count and usually by marrow films showing diminished erythropoiesis and vacuolation of erythroblasts. Thrombocytopenia was also seen in 4 patients and leucopenia in 1. Stopping the drug and transfusing blood or packed cells seems to have led to immediate improvement in the marrow condition except in 2 patients who died of other causes at an early stage. The author concludes that chloramphenicol should not be used for trivial indications, and that when it is given there should be serial reticulocyte counts. A fall in this count demands a marrow film, and if diminished erythropoiesis is verified by this the drug should be stopped. *L. P. Garrod*

VOSTI, G. J., WILLETT, F. M. & JAWETZ, E. **Demethylchlortetracycline. A Clinical Evaluation.** *Clin. Pharmacol. & Therap.* St. Louis. 1961, Jan.–Feb., v. 2, No. 1, 29–39.

This is a general account of clinical experience with demethylchlortetracycline, and not in any sense of a controlled trial. It conveys an impression of damning with faint praise, but the clinical material is so heterogeneous, many of the patients having multiple diagnoses (including malignant disease, diabetes, cardiac infarction, leukaemia and delirium tremens), that the brief particulars given do not enable the reader to reach any decided conclusion of his own. Not even patients' ages are given in the tabulated particulars of each case. These were 37 cases of pneumonia with 9 deaths, some apparently due to causes other than the infection: only 9 of these were shown to pneumococcal, while 2 were staphylococcal and 5 associated with coliform bacilli, no pathogens being found in the remainder. Delayed resolution and superinfection with resistant staphylococci were seen in a few cases. Of 12 cases of urinary tract infection, 1 was classed as cured and 6 as improved (all these 6 had sterile urines, including 2 whose urines were sterile before treatment).

The third series are referred to as skin infections, but the main diagnoses given in the table are cellulitis (7), abscess (2) and fever of unknown origin (2): most of these were "cured" in the table, but according to the text the drug was given "without significant effect or evaluable results". Some tests of bacterial sensitivity were done, and organisms were found to be either "very sensitive or completely resistant" (the highest minimum inhibitory concentration mentioned is over 10 μgm. per ml.). Patients with infections due to sensitive bacteria responded better. Gastro-intestinal disturbances were common, especially in patients given more than 600 mgm. daily, and the results of various function tests convey "a suggestion of renal and hepatic toxicity" which "requires further investigation". *L. P. Garrod*

LIMSON, B. M. **Efficacy of Demethylchlortetracycline in Severe Systemic Infections. Laboratory and Clinical Studies.** *Antibiotic Med.* New York. 1961, Feb., v. 8, No. 2, 98–106. [12 refs.]

This paper from the Philippines reports almost unfailing success in the treatment of 35 patients with demethylchlortetracycline. It was given in doses varying between 300 mgm. every 12 hours to 450 mgm. every 4 hours, and estimations of blood levels, which were made in 21 patients, showed that the former dose gave a level of 1·56–6·25 μgm./ml., and the latter one of 25 μgm./ml. Some estimations in bile and cerebrospinal fluid were also carried out.

Particulars are given of the susceptibility of 34 strains of various Gram positive cocci and 38 of Gram negative bacilli, comparison being made with tetracycline, which was usually less active with a 2- or 4-fold difference. The successfully treated patients comprised 8 with streptococcal sore throat, 10 with pneumococcal pneumonia, 8 with pyelonephritis, 2 with liver abscess due to "microaerophilic enterococci" and 1 to *Escherichia coli*, 1 with enterococcal infection of the gall bladder, 1 with staphylococcal cerebellar abscess, 1 with staphylococcal empyema and 1 with *Streptococcus viridans* endocarditis. The only failures were 1 case of pyelonephritis and 1 of pneumococcal endocarditis. Short histories are given of 7 of the more peculiar of these cases.

L. P. Garrod

SHAPIRO, J. L. & PHILLIPS, F. M. **Demethylchlortetracycline in Clinical Practice. Results of Mass Clinical Field Trials and Description of Electronic Data Processing Methods used in Tabulation and Analysis.** *J. Amer. Med. Ass.* 1961, May 20, v. 176, No. 7, 596–602, 2 figs. [25 refs.]

Case report forms were supplied to about 1,000 practising doctors in various parts of the U.S.A. and Canada in an endeavour to obtain data on a large scale about the effects of treatment with demethylchlortetracycline. At the time of writing about 400 had responded, giving information about 4,704 patients, which was analysed in a computer. This enables the authors to state what percentages of patients were cured or improved who had diseases of different systems (the highest cure rate was in respiratory and the lowest in genito-urinary infections), in different varieties of infections in some of these systems, and according to the nature of the infection (organisms were cultivated in 1,764 patients). Information about side-effects, which occurred in 9·6% of patients and mainly involved the digestive system, are also analysed. There were 721 patients who responded to this treatment after unsuccessful treatment with other antibacterial drugs, and 112 in whom the converse occurred. [The case report form is not reproduced, nor are the criteria of cure or improvement specified. The absolute significance of these findings is doubtful: in so far as they compare therapeutic effect in different conditions the relative results presumably have some validity.]

L. P. Garrod

MCVEIGH, Ilda & REYES, C. R. **A New Species of Streptomyces and its Antibiotic Activity.** *Antibiotics & Chemotherapy.* New York. 1961, May, v. 11, No. 5, 312–19, 1 fig. [15 refs.]

A description is given of the morphological, physiological, and cultural characteristics of a new species of *Streptomyces* for which the name *Streptomyces nashvillensis* is proposed.

It produces an antibacterial substance inhibitory to Gram-positive bacteria.

J. Applied Bact. 1960, Aug., v. 23, No. 2, 318–71, 2 figs. & 1 pl. [Numerous refs.] **Symposium on Methods for the Evaluation of the Antibacterial Activity of Surface Active Compounds.**

This symposium consists of 4 papers.

1. J. G. Davis. *Methods for the evaluation of the antibacterial activity of surface active compounds: technical aspects of the problem* (pp. 319–334). This is an extensive review beginning with a classification of surface-active compounds into cationic (with poor detergent but good germicidal activity), anionic and non-ionic (in which these properties are reversed), and ampholytic, with good detergent and, "it is claimed", good germicidal properties. Types of test are also classified into 4: those involving complete kill, including the phenol coefficient method, those determining rate of kill, either in suspensions or on surfaces, agar diffusion methods and tests measuring interference with metabolic activity. Factors influencing tests include those involving the organism, notably its species and the inoculum size, the medium, its quality in water, *p*H, temperature, the nature and quantity of organic matter, etc. Methods of inactivating the germicide at the end of the period of exposure are referred to, but the author seems uncertain whether this is good practice. In discussing the applicability of the phenol coefficient test it is suggested that comparison should be made not with phenol, but with a standard substance of like composition. His general view is that no single test will serve for this purpose, that standard tests applicable to different types of use are desirable, and that the nearer conditions of test approach those of actual use the better.

2. B. A. Newton. *The mechanism of the bactericidal action of surface active compounds: a summary* (pp. 345–349). This is indeed only a summary of work by the author himself, Salton [this *Bulletin*, 1951, v. 26, 1023] and others, showing that the action of these compounds is to increase the permeability of the bacterial cell, some evidence pointing to action on the cell wall proper and some to an effect on the protoplast membrane. It is also uncertain whether the action is a direct physical one or dependent on the inhibition of enzymes concerned in maintaining the integrity of this structure.

3. Betty C. Hobbs, N. Emberley, Helen M. Pryor and Muriel E. Smith. *The assessment of the activities of surface active agents for use in the catering industry* (p. 350–358). This paper describes and gives the results of a series of tests applied to soap, sodium carbonate, several types of surface-active compound and other sanitizing agents used in the catering industry. Cleansing efficiency was estimated by treating a glass surface soiled with a complex mixture of fats, proteins, and black inks, and measuring subsequent light transmission: soap flakes and certain powders did best at this. Tests of bactericidal efficiency were done by a simple suspension method with *Escherichia coli* and *Staphylococcus aureus* and apparently no neutralizers: cationic compounds were the most active. These also performed best as measured by bacterial counts of dishwashing water in a canteen where each of these substances was in use. It was shown that *Salmonella paratyphi B* will not only survive but sometimes multiply in used dish-water. [None of the surface-active and other presumably proprietary substances used in these tests is named.]

4. Christina M. Cousins, W. A. Hoy and L. F. L. Clegg. *The evaluation of surface active disinfectants for use in milk production* (p. 359–371). This paper describes in detail 2 tests employed at the National Institute for Research in Dairying, Reading. One is the Hoy Can Test, and consists essentially of cleaning and sterilizing a 5-gallon can, contaminating the interior with raw milk, incubated at 22°C. until it has a short methylene blue reduction time, allowing the film of milk to dry overnight, adding the disinfectant to be tested and compared with a standard hyochlorite solution, neutralizing it after 2 minutes, draining, rinsing and rubbing with a rubber squeegee, and counting in this rinse-water the total bacteria, coli-aerogenes and milk-souring bacteria. [An objection to this method would appear to be that there is no control over the numbers of such bacteria in the simple raw milk used for inoculation.] The second is a suspension method with *Escherichia coli*, 10% of homogenized sterile milk as organic matter and a contact time of 2 minutes at 44°C. Many examples of results obtained by these 2 methods are given and compared: they do not necessarily tally because the can test demands both detergent and germicidal action and the second (which in fact is used as a screening test) germicidal only.

L. P. Garrod

Jacobs, S. E. & Harris, N. D. **The Effect of Environmental Conditions on the Viability and Growth of Bacteria damaged by Phenols.** *J. Applied Bact.* 1960, Aug., v. 23, No. 2, 294–317. [Numerous refs.]

This paper describes a very extensive study of the effect of medium composition on the growth of bacteria damaged by phenols. The organisms used were *Escherichia coli* and *Staphylococcus aureus*, which were exposed to 1% phenol, 0·4% *o*-cresol or 0·075% *p*-chloro-*m*-cresol, the action of which was arrested by 200-fold dilution, the growth behaviour of the survivors then being compared with that of untreated bacteria, either by viable counts or by observations of the time taken to reach turbidity. The argument derives from the observation that the addition of Norit (activated charcoal) to broth favours the growth of bacteria damaged by phenol [this *Bulletin*, 1955, v. 30, 430], supposedly by absorbing carried-over phenol itself. [Ferric chloride has been credited with similar action, but did not act like Norit in the experiments described here.] Observations were made on the behaviour of damaged bacteria in tap-water containing Norit, and on their growth in media containing it. The growth-promoting effect in the medium was confirmed, but this is believed to be due to removal of toxic substances in the medium itself and not the phenol. These may be cations: Norit was found to absorb lead, tin, copper, zinc, silver and cobalt from broth. In this connexion it was shown that Mg^{++} favoured the survival of damaged *E. coli* but not that of *Staph. aureus*. The possibility of the presence of toxic substances of other kinds is suggested by the finding that growth is favoured by the extraction of the peptone or meat extract with pyridine before preparation of the medium: these results are complicated by the fact that this process also removes nutrients. The growth of damaged cells was favoured by

lower temperatures, with some difference in optimum between the 2 species, and was very poor or failed at 44°C. *L. P. Garrod*

SCHNEIDER, W., HUBER, M., KWOCZEK, J. J., MUTSCHLER, W. & POPP, W. Über ein neuartiges Desinfektionsmittel für Mineralölemulsionen (Bohröle, Schleiföle). **[A New Type of Disinfectant for Emulsions of Mineral Oils (Boring and Grinding Oils)]** *Berufsdermatosen.* Aulendorf. 1961, Apr., v. 9, No. 2, 57–64.

Grinding and boring oils are emulsions which become heavily contaminated with bacteria with 2 undesirable effects, decomposition and the production of a foul odour, and dermatitis in the operative. This paper is in praise of "Grotan Konz B" (Schülke and Mayr) a disinfectant for addition to such oils, which is described only as "a triazine derivative in combination with other highly active disinfectant substances". It was tested in 4 works (including Daimler-Benz and Brown-Boveri) in midsummer, when decomposition of the oil is usually at its worst. Untreated boring oil emulsion gave counts rising to many thousands of millions per ml. (if these figures are correct it seems to be a better culture medium than many used in the laboratory) and when treated with another (unnamed) disinfectant the counts were also very high, but with the new disinfectant the count was usually zero and never exceeded 90 per ml. even in 34 days' use. Naturally no offensive smells developed, and the material was perfectly tolerated by the skin: it was also proved by patch tests using it at 1%, whereas the concentration added to the oil is only 0·15%. [This paper would be more interesting if one had even a vague general idea what this disinfectant contains. The paper does not even reveal whether it is a solid or a liquid.] *L. P. Garrod*

FALLON, R. J. **Steam Penetration into Containers for Surgical Dressings.** *Lancet.* 1961, July 1, 41–3, 5 figs.

Multiple thermocouple measurements were used to investigate penetration by steam into a standard load of cotton towels packed in a cylindrical drum, a rectangular metal dressing box with fabric filters (Konrich type) [this *Bulletin*, 1960, v. 35, 67], a cardboard box, and as packs wrapped in cotton twill, paper or nylon film. The sterilizer operated by downward displacement at 20 lb. per sq. in. (126°C.). Penetration times in the drum ranged from 5 to 15 minutes; in the metal box this was extended to 30 minutes; further experiments showed that the delay was caused by the filter material and not by the design of the box; the cardboard box showed a delay of 25 minutes. At 17 lb. per sq. in. (123°C.) these delay periods were all increased, the metal box taking 40 minutes to reach the correct temperature.

Preliminary experiments having shown that nylon packs were permeable to steam, the delay was measured and found to be more than with the drum—about 20 minutes. Cloth- and paper-wrapped packs took only slightly longer than the drum.

The author concludes that downward displacement sterilizers (which may need to be used by hospitals for some time longer) can be used with safety, but only if careful attention is given not only to loading but also to packing, so that the penetration time can be allowed for. He emphasizes that only the high-vacuum method can deal with overpacking and the many different containers used in hospitals.

[It is not sufficiently appreciated that the Rectangular Metal Boxes specified in British Standard 3281:1960 are intended only for use in high-vacuum steam sterilizers.] *J. C. Kelsey*

DINEEN, P. **The "Sterilization" of Endoscopic Instruments.** *J. Amer. Med. Ass.* 1961, June 3, v. 176, No. 9, 772–5, 3 figs.

Formalin cabinets and the pasteurization technique of FRANCIS (*Proc. Roy. Soc. Med.*, 1959, v. 52, 998) were compared. The cabinets failed to sterilize simple cultures of tubercle bacilli, *Proteus* or *Pseudomonas* even when large numbers of paraformaldehyde tablets were used and exposure was prolonged to 20 hours. There was some reduction in the number of surviving cultures of *Escherihia coli* and *Staphylococcus aureus.* The cabinets were heated to an unspecified temperature but the addition of moisture is not mentioned. There was a total failure to sterilize either organisms placed in the centres of small packs or instruments contaminated with *E. coli, Aerobacter aerogenes, Ps. pyocyanea, Proteus vulgaris* or *Staph. aureus.*

The pasteurizing technique was tested both by immersing broth cultures in a controlled-temperature water-bath and by using contaminated instruments. Broth cultures of *Staph. aureus, E. coli, Aerobacter aerogenes, Proteus vulgaris* and *Pseudomonas pyocyanea* were killed after 20 minutes' exposure at 85°C.: tubercle bacilli required 60 minutes. Enterococci showed a rapid drop in numbers during the first hour but a "hard core" remained of organisms which were heat resistant at this level. Instruments, including cystoscopes, were all rendered sterile by 20 minutes at 85°C., except those contaminated with enterococci, which needed an hour (there is a discrepancy between the text and a table on this point). Tubercle bacilli were not used in this test. The cystoscopes which had been made with specially heat-resistant cement were unharmed by this treatment.

The author concludes that formalin cabinets do no more than prevent the multiplication of organisms and cannot be relied upon to provide safe instruments. In contrast, if instruments are immersed in water at 85°C for 20 minutes all the common pathogens are destroyed —if the process is extended to one hour all tubercle bacilli and enterococci will be killed as well.

[The temperature recommended in this paper is higher than that used by Francis, and could not be used for all endoscopic instruments. Had the technique been described in greater detail it might have been possible to consider the reason for the discrepancy.] *J. C. Kelsey*

BACTERIA

The order in this section is:—**Cocci; Donovania; Mycobacterium; Corynebacterium; Haemophilus; Pseudomonas; Pfeifferella; Enteric Organisms; Brucella; Pasteurella; Bacillus; Anaerobes; Spirochaetes; Erysipelothrix; Listeria; Others.**

LOSTIA, G. B. Sulla possibilità di impiego di un nuovo terreno per lo stafilococco enterotossico. [**The Possibility of Using a New Medium for Enterotoxic Staphylococcus**] *Giorn. di Batteriol. Virol. ed Immunol.* 1960, Nov.–Dec., v. 53, Nos. 11/12, 420–29. [Numerous refs.] English summary (6 lines).

A medium was devised containing materials similar to those of foods on which the enterotoxic strains of *Staphylococcus* usually produce toxins. 1 gm. of peptone and 1 gm. of lecithin were dissolved in 75 ml. of spring water to which 25 ml. of skimmed milk had been added; *p*H was adjusted to 7·2 and the medium sterilized by tyndallization. Staphylococci were then grown for 6 days at 37°C. in 50 ml. of this medium. Tests were carried out on the fluid medium which had been centrifuged at 3,000 r.p.m. for 5 minutes to remove coagulated particles, filtered (in some cases) and heated at 95°C. for 30 minutes to destroy alpha and beta toxins. 4 ml. of this, warmed to 37°C. was then injected intraperitoneally in each of three kittens, which had been fed an hour before. 4 enterotoxic strains produced typical results in each animal within 10 minutes. Out of 7 strains isolated from foodstuffs which were not suspected of having caused food poisoning, 2 gave rise only in some animals to very slight symptoms. 4 strains considered to be saprophytic produced no symptoms at all.

Filtrate from known toxic strains was used to produce immune sera by injecting rising doses (0·25, 0·5, 0·75, 1·0, 1·5, 2·0, 3·0 ml.) intravenously in rabbits. Such sera reacted specifically with toxic filtrate and also with living staphylococci, though in this case reactions did not exactly match those with the filtrate. *E. Agius*

SCHNEIERSON, S. S., AMSTERDAM, D. & PERLMAN, E. **Enhancement of Intraperitoneal Staphylococcal Virulence for Mice with Different Bile Salts.** [Correspondence.] *Nature.* 1961, May 27, v. 190, 829–30.

Mice were inoculated intraperitoneally with 0·5 ml. of a watery solution of various bile salts, followed immediately by 0·3 ml. of an overnight culture of a *Staphylococcus aureus*. The same dose of organisms, given alone, killed none of 10 mice, and given in 5% gastric mucin killed all of 10. 0·25% sodium deoxycholate was sufficient to enable the staphylococcus to kill all of 10 mice; 1% of most other bile salts had the same effect, but even 4% of sodium dehydrocholate had no potentiating effect. It is suggested that the effects of bile salts are related to their power of lowering surface tension.

R. E. O. Williams

DOOLEY, E. S. **Bacteriophage Impregnated Disk with a Redox Indicator for Rapid Typing of Resistant Strains of *Staphylococcus aureus*.** *J. Lab. & Clin. Med.* 1961, May, v. 57, No. 5, 807–12, 1 fig. [21 refs.]

A method of staphylococcal phage typing employing filter paper disks impregnated with bacteriophage and a redox indicator is described. Sterile filter paper disks are impregnated with 2,3,5 triphenol tetrazolium chloride and dried *in vacuo*. Staphylococcus typing phage suspended in ovalbumin broth is added to each disk. Each receives about 10^7 particles in 0·2 ml. (equivalent to 5,000 routine test doses [RTD]). Disks are dried rapidly *in vacuo* and stored for 3 days over drying agents.

Disks containing the basic set of typing phages are placed on a plate and 0·2 ml. of the strain under test is placed on each disk. Plates are incubated at 37°C. for 4–6 hours until a control disk shows maximum colour development due to growth of the strain.

The phage patterns of 40 strains typed by the conventional method and the disk method are given and the results are identical in 39 of them. [This is remarkable as the reviewer has been unable to achieve such good agreement in typing 40 unselected strains twice by the conventional method, using identical materials and phage dilutions. Several strains are of the same pattern and it is noteworthy that no strain gives minor reactions indicated by a + by most laboratories; at least 50% strains routinely typed show these minor reactions which are of value in grouping sets of strains. There is no indication if the results with the conventional method were obtained with phages at RTD or RTD × 1,000 although the patterns, *i.e.* 3A/53, suggest that at least some were obtained with the concentrated preparations. The typing pattern of a strain depends to a large extent upon the titre of the phages applied. This is uncontrolled by the disk method and indeed the author states that excess phage is necessary. The reviewer feels that the disk method is quite unsuitable for application to staphylococcus phage typing. Its use by workers with no experience of conventional typing method might well hinder rather than help the elucidation of staphylococcal epidemiological problems.] *M. Patricia Jevons*

GULLOTTI, A. & SPANÒ, C. **Phage-Typing of *Staphylococcus aureus* from Different Sources.** *Zent. f. Bakt.* I. Abt. Orig. 1961, v. 181, No. 4, 482–8.

125 strains of *Staph. aureus* were examined for phage type. Of 65 strains from foodstuffs implicated in staphylococcal food-poisoning incidents and 19 from other associated sources, 48 fell into phage Group III and 28 were untypable. Several different patterns within Goup III were observed. Of 42 staphylococci from material not associated with food-poisoning, only 7 were in Group III; 10 were Group I, including 9 of 11 strains from pus.

R. E. O. Williams

SAKURAI, N., UPDYKE, Elaine L., NAHMIAS, A. J. & GERHARDT, Mary R. **Laboratory Observations on the Lysogenic Properties of Hospital Staphylococci and Their Possible Epidemiological Implications.** *Amer. J. Pub. Health.* 1961, Apr., v. 51, No. 4, 566–76. [15 refs.]

The authors investigated the effect of lysogenicity on the typing pattern of strains of staphylococcus of phage type 80/81 and of related types.

In vitro lysogenization was carried out on strains of phage type 80/81, 52/52A/80 and 52/52A/80/81 by using temperate phages derived from strains of phage type 52/52A/80 or 52/52A/80/81. Three phages isolated from strains of phage type 52/52A/80 were capable of changing the typing pattern of strains of type 80/81 or 52/52A/80/81 to type 50/52A/80; these 3 phages differed from one another in their immunity pattern. Two phages isolated from strains of phage type 52/52A/80/81 were found to change strains of phage type 80/81 and 52/52A/80 to phage type 52/52A/80/81; these two phages also differed from one another in their immunity pattern. These results confirm those reported previously [see ROUNTREE, this *Bulletin*, 1959, v. 34, 1174, ASHESHOV and RIPPON, *ibid.*, 1959, v. 34, 1175, COMTOIS, *ibid.*, 1961, v. 36, 287]. Another phage, S. 90, derived from a strain of phage type 80 was found to be capable of changing the type pattern of 3 different strains of phage type 52/52A/80/81 to type 80/81.

The epidemiological significance of these findings is discussed and the authors suggest that, in tracing the spread of staphylococci in epidemics, the isolation and identification of temperate phages carried by the strains may be necessary in order to determine the true relationship between different but apparently related strains.

M. Patricia Jevons

ASHESHOV, Elizabeth H. **A Rapid Screening Test for Phage-Type 80 Staphylococci.** *J. Path. & Bact.* 1961, Apr., v. 81, No. 2, 543–7.

A test is described for the recognition of small numbers of staphylococci sensitive to phage 80 in pathological specimens, within 24 hours of collection. Phage 80 is added to broth inoculated with the specimen to be tested. After 5–7 hours' incubation the broth is tested for phage multiplication. Increase of phage indicates the presence in the broth of staphylococci sensitive to the added phage.

The fact that staphylococcal phages are not type-specific limits the use of the test. Only 50% of strains lysed by phage 80, which were tested from routine hospital material were lysed by this phage alone. A negative result therefore requires no confirmation but strains from positive tests require typing by conventional techniques. The use of this test in screening carriers or cases in an outbreak of infection due to type 80 strains is discussed, as is the application of this technique to material from epidemics due to other phage types of staphylococci. *M. Patricia Jevons*

POPOVICI, Marcella, NESTORESCU, N., ALEXENCO, Ecaterina & FILOTTI, Aurica. Untersuchungen über die Empfindlichkeit nichttypisierbarer Staphylokokken gegenüber einigen zusätzlichen Phagen. **[Investigations of the Susceptibility to Additional Phages of Staphylococci untypable by Standard Phages]** *Zent. f. Bakt.* I Abt. Orig. 1961, v. 181, No. 4, 489–92, 2 figs.

Of 625 strains of *Staph. aureus* all but 61 (9·7%) were typable with the standard set of phages used either at routine test dose [RTD] or at a concentration 1,000 times stronger than RTD. These strains were tested with 13 additional phages and 31 proved sensitive to 1 or more. Phage 44 was the most frequently active, followed by 81 and 42B. [The extent to which the various strains tested were truly independent is not discussed.]

R. E. O. Williams

MILCH, Hedda, EÖRSI, Maria & BOGÁRDI, M. **The Incidence of Staphylococci in Hospital Personnel and Patients, as studied by Phage-Typing.** *Acta Microbiologica.* Budapest. 1960, v. 7, No. 3, 285–96, 2 figs. [26 refs.]

The staphylococcal nasal carriage rate of patients and staff in a children's hospital in Budapest was studied during a 3-month period. Of the 166 children examined 10·2% were carriers on admission, 50% became carriers within 6 days, a total of 71% became positive during their stay in hospital. The carrier rate amongst the staff was 60·6%.

Strains of phage Group I were most common in staff and patients (41%) 26·7% of strains from nurses were of Group II compared with 6·3% of strains from patients; 15·4% of patients' strains were of Group III compared with 2·1% of nurses' strains. On repeated examination 51% of patients' strains and 66% of nurses' strains showed no change throughout the study, but 39% of the patients' strains and 17% of the nurses' strains showed variations in phage groups.

Strains of Group III were most resistant to antibiotics and in the majority of cases change in antibiotic pattern of strains isolated from a single patient was accompanied by a different phage pattern, indicating the acquisition of a different strain. *M. Patricia Jevons*

HOEPRICH, P. D. **Intracommunity Admixture of Human Associated Staphylococci.** *J. Lab. & Clin. Med.* 1961, May, v. 57, No. 5, 781–806, 9 figs. [37 refs.]

Staphylococci capable of forming jet-black colonies on a tellurite-glycine agar [a test regarded as identifying potentially pathogenic staphylococci] were isolated from 59 carriers among normal hospital personnel and from 68 high school seniors; and from 55 patients acquiring staphylococcal infection in hospital and 60 patients infected outside hospital. The staphylococci were tested for ability to produce haemolysins and various enzymes, for sensitivity to 15 different antibiotics, and for phage type.

There were remarkably few differences between the groups of strains in any of the tests and in particular there was no consistent indication that the strains from outside the hospital were less often resistant to antibiotics than the hospital strains. There were some differences in the phage-type distributions. The results are discussed in relation to the idea that exposure to antibiotics in hospital should select the more resistant strains, while residence outside hospital should favour the sensitive, and it is concluded that "As recently as 1959, admixture of human associated staphylococci was not complete in Salt Lake City". *R. E. O. Williams*

GREER, J. E., MENARD, R. R. & LIVINGOOD, C. S., with the technical assistance of Marlene A. BAKER. **Some Bacteriological Data on Dermatological Patients. I. Antibiograms and Phage Types of Staphylococci.** *J. Investigative Dermat.* 1961, Apr., v. 36, No. 4, 273–81. [18 refs.] Discussion 281–2.

Results are given of phage type and antibiogram of strains of coagulase positive staphylococci isolated from out-patients and in-patients in a dermatological department from 1955 to 1960. Antibiograms are recorded numerically (see GREER, *Antibiotics Annual*, 1958–59, 881; *Amer. J. Med. Techn.*, 1959, v. 25, 398). 2,545 separate strains from 2,016 patients were examined. The percentage of antibiotic-resistant strains remained the same throughout the period of study. 60% were resistant to penicillin, with about 30% resistant to penicillin only.

When 849 strains from 576 patients were analysed according to the diagnosis and source of strain, results showed that strains from patients with furunculosis included more antibiotic-resistant strains, and strains of type 80/81, than those from patients with other diagnoses.

Staphylococcus aureus was isolated from nose or lesion of 234 out-patients, from both sites in two-thirds of them and 80% of these had identical strains in both sites. 154 patients were examined before and after admission to hospital. 10% acquired different strains after hospitalization but only 2 patients developed infections. *M. Patricia Jevons*

KERR, J. F. R. **The Antibiotic Sensitivity of *Staphylococcus aureus* in the Brisbane Hospital during 1959.** *Med. J. Australia.* 1961, Apr. 15, v. 1, No. 15, 556–8.

The antibiotic sensitivity of coagulase positive staphylococci isolated from lesions in the Brisbane Hospital during 1959 was assessed by using Evans "Sentest" tablets. Of the 1,081 strains from in-patients 86% were resistant to penicillin, 19% to streptomycin, 1·6% to chloramphenicol, 42% to tetracycline and 0·7% to erythromycin. Corresponding figures for the 1,591 strains from casualty patients were 64%, 1·3%, 0·0%, 6·6% and 0·2%, which were considered to give a good indication of condition in general practice since the casualty department did not treat patients recently discharged from hospital.

Of the 19% (204) in-patient strains resistant to streptomycin 80% were resistant to tetracycline also. 13 of the 17 in-patient strains resistant to chloramphenicol were sensitive only to erythromycin and most of these were from lesions which could have been acquired in hospital. The significantly higher tetracycline resistance rate of in-patient strains (42% compared with 6·6%) is correlated with the widespread use of that drug in the hospital and the similarity in the erythromycin rates between the 2 sets of material (0·7% and 0·2%) indicates the success of the policy of the restricted use of erythromycin which is practised in the hospital.

M. Patricia Jevons

DINEEN, P. **A Period of Unusual Microbial Susceptibility in an Experimental Staphylococcal Infection.** *J. Infect. Dis.* 1961, Mar.–Apr., v. 108, No. 2, 174–80, 8 figs.

In a series of experimental staphylococcal infections in mice the time and dosage of streptomycin were varied and the progress of the disease was assessed by sacrificing surviving animals and counting colonies developing on pour plates prepared from homogenized kidneys. All experiments were carried out with the streptomycin sensitive strain *Staph. aureus*, Giorgio, known to behave in a reproducible manner.

One injection of streptomycin 2 hours after challenge was found to be as effective as continuous treatment begun at that time, and all animals survived. If treatment was delayed for 48 hours all animals given a single dose of the drug were dead at 35 days and several animals on continuous treatment had abscesses at autopsy. Results of variation in the time at which streptomycin was given indicated that organisms were most vulnerable 1 hour after challenge and variations in the dose of drug suggested that 4 mgm. was the most effective single dose. Variation in the challenge dose showed that animals were capable of clearing the tissues of $1{\cdot}6 \times 10$ organisms. *M. Patricia Jevons*

KASHIBA, S., NOZU, H., MIYAMA, A., TANAKA, S. & AMANO, T. **The Antibacterial Action of Spleen and Liver Extracts on Pathogenic Staphylococci.** *Biken's J.* Osaka. 1960, Dec., v. 3, No. 4, 301–12.

Guineapig lungs, livers, spleens and kidneys were homogenized in phosphate buffer at *p*H 7·0. Homogenates were frozen, thawed and centrifuged and the supernates, after high speed centrifugation, were passed through a membrane filter.

Crude filtrates were assayed for antistaphylococcal activity by addition of about 200 viable units of coagulase positive *Staphylococcus aureus* (Newman) to dilutions of filtrate. After 2 hours' incubation at 37°C. melted agar was added to each tube and after further incubation a comparison of colony counts of test and control tubes indicated antistaphylococcal activity. The decrease in colony counts could not be explained by bacterial agglutination.

Crude extracts of spleen contained an antistaphylococcal substance detected by this method. Extracts of live

were weakly active, but lung and kidney extracts were inactive. A preparation of liver rich in Kupffer cells was prepared by differential centrifugation and contained the active substance but an extract of macrophages was inactive. The substance was also active against *Escherichia coli, Klebsiella pneumoniae* and *Shigella flexneri* type 2a but no activity could be detected against the salmonella strains tested.

The antibacterial substance was a protein precipitated by 50% saturation with ammonium sulphate or by precipitation at *p*H 4·0. It was not inactivated by 30 minutes at 56°C. at *p*H 7·0 but was destroyed by 100°C. for 10 minutes. *M. Patricia Jevons*

GREENBERG, L., COOPER, Margaret Y. & HEALY, G. M. **Staphylococcus Polyvalent Somatic Antigen Vaccine. Part II. An Improved Method of Preparation.** *Canadian Med. Ass. J.* 1961, Apr. 29, v. 84, No. 17, 945–7.

The vaccine described by GREENBERG and COOPER [this *Bulletin*, 1960, v. 35, 1226], for which staphylococci were lysed by exposure to Dornase, was found to produce rather severe reactions when injected into the skin of human beings. A vaccine has now been made from staphylococci grown on a synthetic medium, which is described, and its use is followed by very many fewer reactions, although its immunizing activity for rabbits is as good as the earlier vaccine.

It has been found that the serum agglutinin level produced in rabbits in response to vaccination is not a guide to the degree of protection against challenge with living staphylococci. Some protection is afforded by immunization with toxoids, but it is not effective against as wide a range of strains as that produced by the authors' polyvalent vaccine, and the protection is thought not to depend on the antitoxin. *R. E. O. Williams*

LIEB, F. L. & BRENNEIS, Berta. Über Proteasen des Staphylokokkus pyogenes aureus. [**The Proteases of *Staph. aureus***] *Arch. f. Hyg. u. Bakt.* 1961, May, v. 145, No. 3, 161–6.

JOHANOVSKÝ, J. Průkaz pyrogenního účinku stafylokokového toxinu na králících a vzniku pyrogenů při účinku toxinu na bunky *in vitro*. [**A Proof of Pyrogenic Effect of Staphylococcal Toxin in Rabbits and of the Origin of Pyrogens at the influencing of Cells *in vitro* by the Toxin**] *Československ. Epidemiol., Mikrobiol., Imunol.* Prague. 1961, v. 10, No. 4, 226–39, 2 graphs. [Numerous refs.] English summary.

KRAUSE, R. M. & MCCARTY, M. **Studies on the Chemical Structure of the Streptococcal Cell Wall I. The Identification of a Mucopeptide in the Cell Walls of Groups A and A-Variant Streptococci.** *J. Exper. Med.* 1961, July 1, v. 114, No. 1, 127–40, 1 fig. on pl. [20 refs.]

(L. 432)

HALBERT, S. P. & KEATINGE, Suzanne L. **The Analysis of Streptococcal Infections. VI. Immunoelectrophoretic Observations on Extracellular Antigens Detectable with Human Antibodies.** *J. Exper. Med.* 1961, June 1, v. 113, No. 6, 1013–28, 7 figs. [28 refs.]

"It has been found by immunoelectrophoresis, that Group A streptococci release at least 20 distinct extracellular antigens in human tissues, as judged by naturally occurring antibodies present in normal pooled human gamma globulin.

"Several of these precipitin arcs have been identified with streptococcal antigens previously purified by electrophoresis and chromatography.

"Human gamma globulin, as well as several rheumatic fever sera, were shown to be remarkably potent in antistreptococcal antibodies, when compared to four horse antibody concentrates obtained by hyperimmunization with several streptococcal filtrates.

"A Group C streptococcal culture concentrate revealed 8 or 9 antigens for which corresponding antibodies were present in human gamma globulin."

ERLANDSON, A. L., Jr. & GAGLIARDI, Leola A. **The Pathogenesis of Experimental Enterococcal Pyelonephritis in Mice.** *J. Infect. Dis.* 1961, Mar.–Apr., v. 108, No. 2, 181–8, 5 figs. [14 refs.]

7 strains of *Streptococcus faecalis* were tested for their ability to produce renal infection after intravenous injection into mice. 1 strain was selected for further work because it killed none of 20 mice and yet established renal infection in 39 of 40. Further tests showed that the dose giving established renal infection at 7 days in 50% of kidneys was about 8×10^6 organisms. Mice inoculated with 10^5 bacteria or fewer and killed immediately yielded no enterococci from the kidneys; for a positive blood culture to be obtained the dose had to be 10^7.

Quantitative bacteriological sampling was performed on the organs of a series of mice inoculated with 10^8 enterococci and killed at intervals. In the kidneys infection persisted for periods of 160 days and more; no other organ showed persistent infection for more than about 50 days.

The persistent infection was only rarely associated with illness in the mice; histological lesions were demonstrable [but are not described]. Enterococci were found in urine samples from practically all the mice showing renal infection at autopsy. *R. E. O. Williams*

BLEIWEIS, A. S. & ZIMMERMAN, L. N. **Formation of Two Types of Osmotically Fragile Bodies from *Streptococcus faecalis* var. *liquefaciens*.** *Canadian J. Microbiol.* Ottawa. 1961, June, v. 7, No. 3, 363–73, 6 figs. [20 refs.]

"Osmotically fragile bodies which may be true protoplasts of the group D *Streptococcus faecalis* var. *liquefaciens* have been produced by use of a lytic enzyme derived from phage-infected cultures fo the group D *S. faecalis* var. *zymogenes*. These bodies may be held in

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1·1 *M* sucrose and are lysed almost quantitatively upon removal into water at room temperature or at 37°C. The phage-associated lysin, in the presence of 0·7 *M* cysteine, causes almost complete lysis of the sensitive organism by the end of 1 hour at 37°C. and effects complete removal of cell-wall materials (rhamnose-containing moieties and phage-receptor sites) in that time.

"Osmotically fragile bodies which may be termed spheroplasts of *S. faecalis* var. *liquefaciens* have been produced by the use of lysozyme on cells previously grown in penicillin (5 units/ml.). Lysis to the extent of 50% in 1 hour at 37°C. occurs in the aqueous suspensions, whereas 17% sucrose with 0·2% $MgSO_4.7H_2O$ or 0·2% $MgSO_4.7H_2O$ alone effects almost complete stabilization. The stabilized bodies are lysed almost quantitatively upon removal to water at 56°C. Cell-wall material containing rhamnose remains on these forms, indicating that they are spheroplasts rather than protoplasts."

BERGER, U. Zur Variabilität der Zuckervergärungen durch Neisserien. **[Variation in Sugar Utilization by *Neisseria*]** *Arch. f. Hyg. u. Bakt.* 1961, June, v. 145, No. 4, 296–301. [10 refs.]

The English summary appended to the paper is as follows:—

"24 strains of Neisseria, belonging to 5 different species, were tested with respect to their variability in fermenting sugars, as reported in the literature. The investigations were carried out over a period of from 4 to 18 months. Glucose, maltose, fructose, and saccharose were offered in the Lingelsheim plate. It was observed that in one-third of the strains the utilization of the monosaccharides, especially glucose, was irregular while all strains showed a constant and regular behaviour towards the disaccharides."

The species were: *N. perflava, flava, subflava, sicca* and *animalis.*

BUBE, F. W. Die Beschleunigung der bakteriellen Tuberkulose-Diagnostik mit Hilfe von Triphenyltetrazoliumchlorid. **[Acceleration of the Bacterial Diagnosis of Tuberculosis by means of Triphenyltetrazoliumchloride]** *Zent. f. Bakt.* I. Abt. Orig. 1961, v. 182, No. 1, 85–92, 3 figs. [35 refs.]

If cultures set up on Hohn's solid medium for *Myco. tuberculosis* are sprayed with a solution of tetrazolium chloride containing 50 mgm.% the early colonies both of human and bovine strains take on a red colour from reduction of the colourless tetrazolium and it is possible in this way to recognize the development of these colonies on the average 4 days earlier than without this procedure. The presence of glycerin in the medium is essential and the development of colour is also promoted by the presence of diphosphopyridine nucleotide.

J. W. McLeod

KERTAY, N. & FODOR, T. Wirkung von Mucin un Dextran Präparaten auf die Tuberkulose vo gleichzeitig Intracutan mit Mycobacterium Tube culosis infizierten Meerschweinchen. **[Effect o the Development of Tuberculosis of Addin Preparations of Mucin or Dextran to Suspen sions of *Mycobacterium Tuberculosis* injecte Intracutaneously to Guineapigs]** *Acta Tube culosea Scandinavica.* 1961, v. 40, No. 2, 145–9.

The strain of *Mycobacterium tuberculosis* used wa H37Rv. The suspensions of this strain were prepare in normal NaCl solution and in 5% mucin or Dextran these suspensions were injected intracutaneously in di ferent areas of the skin of the same animal and the exter and speed of development of the lesions were observe

The largest lesions appeared where Dextran was use and even those following injection of tubercle bacil suspended in mucin were twice as large as those obtaine with suspensions in saline. Lesions appeared at least week sooner than in the control sites when the bacteri were injected with Dextran, and after smaller doses c bacteria with Dextran, as could be demonstrated b injecting graded dilutions of bacteria suspended in salin and Dextran respectively. *J. W. McLeod*

BOTEZ, Virginia, ANGELESCO, I., BONCIU, C., PARASCHI VESCO, Maria & PETROVICI, Monica. Étude ex périmentale sur la vaccination intensive par voi orale avec le vaccin B.C.G. **[An Experimenta Study of Intensive Peroral BCG Immunization** *Arch. Roumaines Path. Expér. et Microbiol.* 196 June, v. 20, No. 2, 171–9. [16 refs.]

The English summary appended to the paper is a follows:—

"An experimental investigation concerning intensiv peroral BCG immunization has led to the followin conclusions:

"1. Intensive peroral immunization of adult guinea pigs with 400 mg. BCG results in a degree of resistanc to tuberculosis which is definitely superior to that in duced by the parenteral (intradermal or percutaneou introduction of the vaccine. For the same total amoun of vaccine, the degree of resistance appears to depen on the number of doses and the rate of their administra tion.

"2. In most cases, repeated doses result in increase percentage rates and intensities of the tuberculin reaction (as compared to the initial ones). Specific resistance i the immunized animals varies in the same direction a these phenomena. No dissociation could be demonstrate between the degree of tuberculin sensitivity and that c protection consequent on immunization.

"3. By transferring these experimental results (wit all due qualifications) to immunization in humans, w may assume that peroral immunization with large vaccin doses administered according to a schedule providin judicious repetition of the antigenic stimuli, affords a efficient and readily performed method of vaccination and hence deserves at least the same attention as th parenteral methods."

BASTARRACHEA, F. & GOLDMAN, D. S. **Diphosphopyridine Nucleotide-Linked Nitrate Reductase from *Mycobacterium tuberculosis*.** *Biochim. et Biophys. Acta.* 1961, June 10, v. 50, No. 1, 174–6, 1 fig. [12 refs.]

SACHSE, H. H. Zur Kultivierung von *C. diphtheriae* aus Patientenmaterial. [**The Cultivation of *Corynebacterium diphtheriae* from Patients**] *Zent. f. Bakt.* I. Abt. Orig. 1961, v. 181, No. 4, 556–60. [14 refs.]

After a preliminary discussion of the complexity of many of the methods of bacteriological diagnosis of diphtheria now used in Germany which tend to cause undesirable delays in reporting, the author describes the methods which he had found most satisfactory in a recent considerable outbreak in the vicinity of Johanngeorgestadt in which 554 strains were isolated.

He recommends Billing's modification of Tinsdale's medium and finds that if used as sloped tubes which are sealed so as to limit access of oxygen the brown haze develops more rapidly around colonies and can be recognized within 24 hours in 25% of positive cases. This justifies a report of suspect diphtheria.

Inoculations to Clauberg's fluid medium were made at the same time and sub-culture to Clauberg and to Tinsdale plates permitted confirmation of the diagnosis in over 90% of cases within 2 days.

In 3 cases only among 700 was a case wrongly reported as diphtheria suspect on account of development of a brown zone around a colony. *J. W. McLeod*

WEISSFEILER, J. & GÁSPÁR, G. Diphtherie-Antitoxinbildung bei weissen Mäusen und Meerschweinchen nach Immunisierung mit verschiedenen Adjuvantien. [**Production of Diphtheria Antitoxin in White Mice and Guineapigs under the Influence of a Variety of adjuvants**] *Ztschr. f. Immunitätsf. u. Exper. Therap.* 1961, May, v. 121, No. 3, 217–23.

4 groups of white mice, animals which are notable for their poor antibody formation to diphtheria toxin, were immunized respectively with (a) diphtheria toxoid 100 Lf, (b) 15 Lf diphtheria toxoid combined with aluminium phosphate gel according to Holt's formula, (c) as (b) with addition of killed BCG, (d) 15 Lf diphtheria toxoid combined with Freund's adjuvant (paraffin oil emulsified with 15% Arlacel, sterilized at 120°C. for 30 minutes and mixed with 0·5 mgm. killed BCG). The production of antitoxin was in the order group (d) > (c) > (b) > (a).

Similar results were obtained in immunizing guineapigs and were rather more pronounced. If living BCG were substituted for dead the antibody yield was still greater. *J. W. McLeod*

KENDRICK, Pearl L., ELDERING, Grace & EVELAND, W. C. **Fluorescent Antibody Techniques. Methods for Identification of *Bordetella pertussis*.** *Amer. J. Dis. Children.* 1961, Feb., v. 101, No. 2, 149–54, 1 fig. [16 refs.]

Pernasal swabs from infants with possible whooping-cough were placed in 0·2 ml. of 1% casamino acids. Within 2 hours the moistened swab was streaked across Bordet-Gengou plates and slide preparations were also made. The inoculated plates were incubated and the slides stained with conjugated pertussis antiserum. The results from 130 pernasal swabs showed 21 to be positive and 98 negative by both the cultural and fluorescent antibody staining technique; 4 were positive by the cultural technique only, whereas the remaining 7 were positive by the fluorescent staining technique only.

Some pitfalls and limitations of the fluorescent antibody technique were revealed and a recommendation is made that both techniques be compared to evaluate the place of the fluorescent antibody technique as an aid in the laboratory diagnosis of the disease.

F. T. Perkins

MANTEN, A., KAMPELMACHER, E. H. & GUINÉE, P. A. M. **Frequency of Resistance to Chloramphenicol and Tetracyclines among 12014 *Salmonella* Strains isolated in 1958 and 1959.** *Antonie van Leeuwenhoek: J. Microbiol. & Serol.* 1961, v. 27, No. 1, 103–9.

These authors from the National Institute of Public Health, Utrecht, first point out that the widespread use of antibiotics both therapeutically in man and as feed supplements in animals might be expected to lead to the appearance of resistant strains of *Salmonella* spp. They collected 12,014 strains of 27 species, 9,477 from human and the rest from various animal sources, and first screened them by cultivation on media containing 25 and 50 μgm./ml. respectively of tetracycline and chloramphenicol. Any which grew were then tested by a tube dilution method (but no results so obtained are given). The number resistant to tetracycline only was 159, to chloramphenicol only was 38, and to both 53, *i.e.*, 250 in all, or 2·08% of the total. [Although the authors do not comment on this, it seems important that of 91 strains of *Salmonella typhi* only 1 was resistant to tetracycline and none to chloramphenicol. Of 446 strains of *Salmonella paratyphi B*, 1 was resistant to each antibiotic only and 13 to both.] There was no species of which no resistant strains were found. Analysis according to source showed nothing significant except a high frequency of resistance in strains from laboratory monkeys, but these had been "treated prophylactically and therapeutically" with both antibiotics.

L. P. Garrod

TINELLI, Regina. Étude sur la méthylation du polyoside somatique extrait de *Salmonella typhi*. [**Methylation of Somatic Polysaccharides Extracted from *Salmonella typhi***] *Bull. Soc. Chimie Biol.* 1961, v. 43, Nos. 2/3, 357–66. [30 refs.]

TOMA, S., SORU, E., BARBER, C., BOGOKOWSKY, B. & GRITAENCO, V. Contribuțiuni la studiul vaccinurilor antitifo-paratifice din extracte microbiene adsorbite pe suport mineral. III. Studiul imunobiologic comparativ al unor extracte antigenice obținute din *S. paratyphi A* si *S. paratyphi B*. [**Contribution to the Study of Typhoid-Paratyphoid Vaccines**

from Bacterial Extracts Adsorbed on a Mineral Support. III. A Comparative Immunobiological Study of Antigenic Extracts Obtained from *Salm. paratyphi A* and *Salm. paratyphi B*] *Studii si Cercetări Inframicrobiol., Microbiol. si Parazitol.* 1958, v. 9, No. 2, 267–74. French summary.

The authors report further investigations of fractions of *Salmonella paratyphi A* and *B* obtained by previously described methods of extraction with hot water and hot trichloroacetic acid [this *Bulletin*, 1959, v. 34, 926]. Precipitating titres of 100,000–400,000 were obtained with trichloroacetic acid extracts, and similar titres could be obtained with aqueous extracts when the time of heating was prolonged to 2 hours. When injected into mice the extracts produced a low degree of immunity to subsequent challenge. In rabbits injected with the extracts intravenously in doses up to 0·5 mgm. adequate titres of O agglutinins of *Salm. paratyphi B* were observed, but the *Salm. paratyphi A* titres were considerably lower. The H agglutinin titres obtained with the aqueous extract were somewhat lower than those obtained in a control experiment with a corpuscular vaccine, and the titres obtained with the trichloroacetic acid extract were much lower. The sera of rabbits injected with *Salm. paratyphi B* extracts of both types conferred adequate immunity in mouse protection tests. In similar experiments extracts prepared from the same organisms by extraction with hydrochloric acid were completely devoid of serological and immunological activity.

D. J. Bauer

Schneider, H., Formal, S. B. & Baron, L. S. **Experimental Genetic Recombination *in vivo* between *Escherichia coli* and *Salmonella typhimurium*.** *J. Exper. Med.* 1961, July 1, v. 114, No. 1, 141–8, 1 fig. [12 refs.]

"Antibiotic-pretreated mice were fed orally an Hfr culture of streptomycin-resistant *E. coli* and 1 day later, a streptomycin-resistance F− *S. typhimurium* culture. Hybrids were recovered in relatively small numbers from the feces of these mice within 24 hours demonstrating that genetic recombination can occur within the intestinal tract of a mammalian host under experimental conditions. These hybrids multiplied rapidly and persisted throughout the course of the experiment. In addition, hybrids were recovered which had not been observed in single matings performed *in vitro*."

Le Minor, L., Le Noc, P. & Dréan, D. Un nouvel antigène somatique des *Salmonella*. **[A New Somatic Antigen in *Salmonella*]** *Ann. Inst. Pasteur.* 1961, July, v. 101, No. 1, 133–4.

The English summary appended to the paper is as follows:—

"Description of a new *Salmonella* serotype (*S. tranoroa*) possessing a new O antigen ($55:k:z_{39}$)."

Van Oye, E., Le Minor, L. & Moinet, J. Une nouve espèce de *Salmonella*: S. Tournai (3,15:y:z **[A New *Salmonella* Species: S. Tournai]** *An Inst. Pasteur.* 1961, July, v. 101, No. 1, 135–6.

The English summary appended to the paper is follows:—

"Description of a new *Salmonella* species, *S. tourn* ($3,15:y:z_6$) isolated from the stools of an infant, thr and a half months old, who suffered from a lig intestinal disorder."

Brede, H. D. Salmonella Woodstock, ein neu Serotyp ($16:z_{42}:1$, (5), 7). **[Salmonella Woo stock, a New Serotype ($16:z_{42}:1$, (5), 7)]** *Zei f. Bakt.* I. Abt. Orig. 1961, v. 182, No. 2, 279–8

Kersten, H. & Rauen, H. M. **Degradation of Deox ribonucleic Acid in *Escherichia coli* Cells treat with Mitomycin C.** [Correspondence.] *Natu* 1961, June 24, v. 190, 1195–6, 1 fig.

Pitts, J. D., Stewart, Janet A. & Crosbie, G. **Observations on Glycine Metabolism in *Esch richia coli*.** *Biochim. et Biophys. Acta.* 196 June 24, v. 50, No. 2, 361–3. [10 refs.]

Dénes, G. **Glucose Repression and the Inductic of β-Galactosidase Synthesis in *Escherichia co*** *Biochim. et Biophys. Acta.* 1961, June 24, v. 5 No. 2, 408–9, 1 fig.

Herzenberg, L. A. **Isolation and Identification Derivatives formed in the Course of Intracellul Accumulation of Thiogalactosides by *Escherich coli*.** *Arch. Biochemistry.* 1961, May, v. 93, No. 314–15.

Berg, P.; Bergmann, F. H.; Ofengand, E. J.; Diec mann, M. **The Enzymic Synthesis of Amin Acyl Derivatives of Ribonucleic Acid. I. T Mechanism of Leucyl-, Valyl-, Isoleucyl-, a Methionyl Ribonucleic Acid Formation** [Ber Bergmann, Ofengand & Dieckmann]. *J. Bi Chem.* 1961, June, v. 236, No. 6, 1726–34, 6 fig [43 refs.] **II. The Preparation of Leucyl-, Valy Isoleucyl-, and Methionyl Ribonucleic Ac Synthetases from *Escherichia coli*** [Bergman Berg & Dieckmann]. *Ibid.*, 1735–40, 3 figs. [refs.] **III. Isolation of Amino Acid-Accept Ribonucleic Acids from *Escherichia coli*** [Ofe gand, Dieckmann & Berg]. *Ibid.*, 1741–7, 6 fig [39 refs.]

Guillaume, J., Osteux, R. & Derieux, J. C. Sur mode d'action des histones "arginine" sur *Esch richia coli*. **[Mode of Action of "Arginine Histones on *Escherichia coli*]** *C.R. Soc. Bi* 1961, v. 155, No. 1, 85–90, 3 figs.

United States Dept. Health, Education & Welfare. **The Biochemical Reactions of Members of the Genus Proteus** [Ewing, W. H., Suassuna, I. & Suassuna, I. R.]. 18 pp. [30 refs.] 1960. Atlanta 22: Pub. Health Service, Communicable Disease Center, Georgia.

The subdivision of the genus into 4 species (*Proteus vulgaris, P. mirabilis, P. morganii* and *P. rettgeri*) proposed by Rustigian and Stuart forms the base line for this monograph. The biochemical reactions of these species reported by earlier workers are shown in tabular form and are compared with the authors' own findings in tests on 255 strains. In general, these confirm the characteristics reported by other workers and their chief interest lies in the results obtained in tests not often applied before.

Almost all strains are positive in MR (at 37°C.), urea, KCN and phenylalanine, and are negative in lactose and dulcitol fermentation and in lysine decarboxylase and arginine dihydrolase. Other tests such as the production of indole, H_2S, gelatinase, ornithine decarboxylase, and maltose fermentation are useful in distinguishing between the species (see table). The authors recommend TSI medium for detecting H_2S; with more sensitive methods the distinguishing value of the test is lost [see Clarke, *J. General Microbiol.*, 1953, v. 8, 397; this *Bulletin*, 1954, v. 29, 186].

	P. vulgaris	*P. mirabilis*	*P. morganii*	*P. rettgeri*
Indole	+	−	+	+
H_2S (TSI)	+	+	−	−
Gelatin	+	+	−	−
Ornithine	−	+	+	−
Maltose	+	−	−	−

S. T. Cowan

Hejzlar, M. & Duniewicz, M. Versuche mit einer verbesserten Technik der Keimanzüchtung bei Brucellosekranken. [**Observations on Brucella Infection; an Improved Culture Technique**] *Zent. f. Bakt.* I. Abt. Orig. 1961, v. 181, No. 4, 493–502. [32 refs.]

Under the designation SBA (semi-synthetic brucella agar) a very complex medium is described containing the antibiotics polymyxin and bacitracin, chick-embryo extract and a number of ingredients which the authors admit are difficult to obtain. On this medium better results were obtained both in respect of growth from small inocula of standard strains and in the isolation of brucella strains from cases of infection than with some of the longer-established media such as Huddleson's liver agar and tryptose agar. Among 18 cases investigated 5 successful isolations were made from sternal marrow and one from venous blood.

The sensitivities of the strains isolated were tried out with a number of antibiotics. They were resistant to penicillin, polymyxin and vancomycin, but peculiarly sensitive to tetracycline. Sensitivity to bacitracin is not mentioned. *J. W. McLeod*

Domaradskii, I. V., Iaromiuk, G. A. & Vasil' Eva, Z. I. **The Relationship between *Pasteurella pestis* and Hyaluronic Acid and on the Presence of a Spreading Factor in this Organism.** *J. Microbiol., Epidemiol. & Immunobiol.* London. 1960, v. 31, No. 7, 1332–7, 2 figs. [Translated from Russian.]

[An abstract of this paper appeared in the *Tropical Diseases Bulletin*, 1961, v. 58, 1130.]

Buckland, F. E. & Treadwell, R. H. **A Comparison of Plague Vaccines by the Mouse Protection Test.** *J. Hygiene.* 1961, Mar., v. 59, No. 1, 49–56.

[An abstract of this paper appeared in the *Tropical Diseases Bulletin*, 1961, v. 58, 1130.]

Dowdle, W. R. & Hansen, P. A. **A Phage-Fluorescent Antiphage Staining System for *Bacillus anthracis*.** *J. Infect. Dis.* 1961, Mar.–Apr., v. 108, No. 2, 125–35, 7 figs. [19 refs.]

Bacillus anthracis cannot be identified by staining it with fluorescent antibody since many other species of *Bacillus* share the same antigens. However, gamma phage lyses *B. anthracis* specifically [Brown *et al.*, this *Bulletin*, 1958, v. 33, 991] and bacterial smears covered with a drop of this phage suspension, washed, and treated with fluorescein-labelled phage antiserum were found to exhibit specific, characteristically speckled, fluorescence. The intensity of staining varied with phage concentration and at least 5×10^7 phage particles per ml. were required before fluorescence was visible. Cultures from 4 hours to a week old could be stained this way, but spores and encapsulated strains could not.

29 strains of *B. anthracis* and 91 strains of 15 saprophytes were tested with phage and fluorescein-labelled phage antiserum and also with fluorescein-labelled antiserum prepared against *B. anthracis*. All the strains of *B. anthracis* were positive by the phage test and the saprophytes were negative, except 4 out of 26 strains of *B. cereus* and 5 out of 10 of *B. cereus* var. *mycoides*. These 9 strains could not be classified as *B. anthracis* according to the criteria of Leise *et al.* [*ibid.*, 1959, v. 34, 1292] and they were not lysed by gamma phage. 43 of the saprophytes reacted with the bacterial antiserum, the organisms staining uniformly in contrast to their speckled appearance with phage antiserum. As well as giving more numerous cross-reactions, fluorescence with antiserum prepared against bacilli or spores was more difficult to interpret and varied, sometimes within the same microscopic field. *Janice Taverne*

Bennett, E. O. & Williams, R. P. **Variation in Nucleic Acid Phosphorus Content between Strains of the Same Species of *Bacillus*.** *Texas Reports on Biol. & Med.* 1961, v. 19, No. 2, 259–67, 1 fig. [13 refs.]

"The deoxyribonucleic acid (DNA) and ribonucleic acid (RNA) phosphorus content of the vegetative cells

of 33 strains of *Bacillus anthracis* and 10 strains of *Bacillus cereus* were determined using the method of Schmidt and Thannhauser. All strains were grown under identical conditions before analysis. Wide variation was found in the content of both species. The DNA content of *B. anthracis* varied from 0·39 μg. P per mg. of dry cells to 1·01 μg. P, with an average value for the 33 determinations of 0·67 μg. P. Avirulent strains contained less DNA than virulent ones. In the case of *B. cereus*, the average DNA content was 0·45 μg. P per mg. of dry cells. The RNA content of *B. anthracis* varied from 2·32 μg. P per mg. of dry cells to 4·45 μg. P. The average content was 3·43 μg. P. The 10 *B. cereus* strains contained an average RNA content of 3·27 μg. P per mg. of dry cells. As would be expected from the DNA and RNA data, the RNA to DNA ratio of individual strains also differed. Multiple determinations of the DNA and RNA content of one strain of *B. anthracis* indicated that there was less variation in this case than when several different strains were examined."

González, C. Étude comparée deux souches de *Cl. tetani* et de leurs formes L (colonie B), obtenues par l'action de la glycine. [**Comparative Study of Two Strains of *Clostridium tetani* and the L Forms derived from them by Cultivation on Media containing Glycine**] *Antonie van Leeuwenhoek: J. Microbiol. & Serol.* 1961, v. 27, No. 1, 19–26, 4 figs.

By cultivation of the strains of tetanus on media containing glycine a modification was obtained which consisted in the alteration of appearance in cultures from the usual colony with radiating outgrowths to a smaller more compact and granular colony. This change in the appearance of the colony was associated with the occurrence of a large proportion of spherical Gram-positive bodies of 2·5–4 μ in diameter and it persisted through many subcultures in media without glycine. The parent and derived strains were not distinguished by changes in biochemical activity, antibiotic resistance or altered capacity to produce toxin. These changes resemble those which have been observed to occur under the influence of penicillin. *J. W. McLeod*

Ispolatovskaya, M. V. & Marmalevskaya, L. Y. **A Study of the Antigenic Composition of *Clostridium perfringens* Toxin and Toxoids.** *J. Microbiol., Epidemiol. & Immunobiol.* London. 1960, v. 31, No. 8, 1489–96, 5 figs. [11 refs.] [Translated from Russian.]

Mailloux, M. & Kolochine-Erber, Berthe. Étude sur le métabolisme des leptospires. Essai de milieu chimiquement défini. [**Studies on Metabolism of Leptospirae. Attempts at Cultivation on a Synthetic Medium**] *Ann. Inst. Pasteur.* 1961, Mar., v. 100, No. 3, 390–95. [19 refs.]

The numbers of media which have been suggested for the culture of leptospires point out the difficulties of this procedure. A major inconvenience is the necessity to include rabbit serum: this interferes with the study of metabolic, nutritive and growth factors. Many attempts have been made to replace rabbit serum by mixtures of chemical components—salts, amino-acids, vitamins—but none have been confirmed as satisfactory. However, it has been shown that rabbit serum contains 2 factors necessary for the growth of leptospires; one can be dialysed, but not the other. Substitutes for these factors are peptone and asparagine for the former and rabbit serum albumin for the latter.

Numerous attempts have been made to find a substance which, when added to a medium containing rabbit serum, will stimulate growth of leptospires. Amino-acids and vitamins (particularly those of "group B") have attracted most attention but the findings have not been conclusive and are often contradictory. Trials of purine and pyrimidine bases have likewise been made; and cyanocobalamine has been substituted for rabbit serum in Korthof's medium.

The authors used Stuart's medium [this *Bulletin*, 1947, v. 22, 284] minus rabbit serum, with added vitamin B12: pathogenic leptospires failed to thrive and finally died out, but saprophytic water leptospires survived (in diminished numbers). Omission of vitamin B12 from the medium resulted in rapid lysis and death of the saprophytic leptospires. The authors conclude that vitamin B12 is a necessary growth factor for all leptospires none of which (including saprophytes) can synthesize it: they subdivide lectospires into 2 groups—pathogens, which require rabbit serum; and saprophytes which do not.

L. H. Turner

Kmety, E. & Bakoss, P. Hämolysin- und Lipaseproduktion bei Leptospiren verschiedener Serotypen. [**Haemolysin and Lipase Production by Leptospirae of Different Serological Groups**] *Zent. f. Bakt.* I. Abt. Orig. 1961, v. 181, No. 4, 503–15.

Although frankly haemolytic strains are met in the *pomona* and *grippo-typhosa* groups and are never encountered in the *australis, ballum* and *celledoni* groups, their occurrence in many other groups was observed but was too irregular to serve as a basis of classification. Lipase production was more widely distributed but also too inconstant within any given serological group to serve the purpose of differentiation. A table which extends to 7 pages and covers 19 serological groups gives the haemolytic and fat-splitting activities of individual strains. *J. W. McLeod*

Mukerjee, S. **Diagnostic Uses of Cholera Bacteriophages.** *J. Hygiene.* 1961, Mar., v. 59, No. 1, 109–15. [20 refs.]

[An abstract of this paper appeared in the *Tropical Diseases Bulletin*, 1961, v. 58, 1131.]

Silverman, S. J., Elwell, Lynn & Kautter, D. A. **A Mortality Enhancing Extract isolated from *Listeria monocytogenes*.** *J. Immunology.* 1961, June, v. 86, No. 6, 669–74. [14 refs.]

"The injection of a crude extract (MEF) prepared from cells of *Listeria monocytogenes* reduced the resistance of mice, guinea pigs, rabbits and rhesus monkeys to infection with *Listeria*. The resistance of mice to a number of other species of bacteria, both Gram-positive and Gram-negative, was also impaired by the cell material. The extract was heat stable when held at temperatures up to 70°C. for 30 min. It was effective when administered prior or subsequent to infection or when injected by a route other than that used for challenge.

"Injection of MEF into guinea pigs caused (a) a loss of weight, (b) changes in body temperature, (c) qualitative and quantitative alteration of the white blood cells, including monocytosis and (d) changes in serum lysozyme, properdin and complement."

RICKETTSIAE

ZARNEA, G., MITRICĂ, Natalia & IONESCO, Honorina. La réaction de précipitation en gel avec des antigènes rickettsiens. [**The Precipitation Reaction in Gel with Rickettsial Antigens**] *Arch. Roumaines Path. Expér. et Microbiol.* 1961, Mar., v. 20, No. 1, 13–19, 2 figs.

[An abstract of this paper appeared in the Tropical *Diseases Bulletin*, 1961, v. 58, 1003.]

WEYER, F. Zur Frage der Widerstandsfähigkeit von Rickettsien im Läusekot gegen physikalische Einflüsse, insbesondere gegen Wärme. [**Capacity for Resistance of Rickettsiae in Louse Faeces against Physical Agencies, especially against Heat**] *Ztschr. f. Tropenmed. u. Parasit.* Stuttgart. 1961, v. 12, No. 1, 78–92.

[An abstract of this paper appeared in the *Tropical Diseases Bulletin*, 1961, v. 58, 1003.]

GIROUD, P., CAPPONI, M. & DUMAS, N. Comparaison entre *Rickettsia sennetsui* et *Rickettsia tsutsugamushi*: morphologie, pouvoir pathogène, pouvoir antigénique. [**Comparison between *Rickettsia sennetsui* and *R. tsutsugamushi***] *Bull. Soc. Path. Exot.* 1960, Nov.–Dec., v. 53, No. 6, 960–65, 2 figs. on pl.

[An abstract of this paper appeared in the *Tropical Diseases Bulletin*, 1961, v. 58, 1004.]

HAZATO, H. & YAMAMOTO, S. **The Effect of Polyvinylpyrrolidone on the Viability of *Rickettsia orientalis in vitro*. I. Storage of the Infective Mouse Tissue Suspension and Intraperitoneal Washings in Refrigerator and in Incubator.** *Japanese J. Exper. Med.* 1960, Dec., v. 30, No. 6, 475–83.

[An abstract of this paper appeared in the *Tropical Diseases Bulletin*, 1961, v. 58, 903.]

URBACH, H. & SCHABINSKI, G. Immunelektrophoretische Untersuchungen an *Rickettsia prowazekii, Coxiella burnetii* und *Proteus OX*-Stämmen. [**Immunoelectrophoretic Investigations of *Rickettsia prowazeki, R. burneti* and *Proteus OX*-Strains**] *Zent. f. Bakt.* I. Abt. Orig. 1960, v. 180, No. 4, 433–41, 6 figs. [23 refs.]

[An abstract of this paper appeared in the *Tropical Diseases Bulletin*, 1961, v. 58, 902.]

BACTERIOPHAGES

MEYNELL, Elinor W. **A Bacteriophage for Motile Bacteria.** [Correspondence.] *Nature.* 1961, May 6, v. 190, 564.

Phage χ adsorbs specifically to motile *Salmonella*, and conditions determining the sensitivity of the bacteria to the phage are described here. Phage χ only adsorbed to flagellated strains and only to those carrying certain flagellar (H) antigens. Strains with most of the H antigens could be sensitive to the phage but strains with antigens of the *g* complex, for instance, whether naturally occurring or prepared by transduction, were resistant. The phage did not absorb to those naturally occurring cells which possessed flagella but which were not motile, or to cells whose flagella had been paralysed by 2,4-dinitrophenol. In electron micrographs phage particles were seen attached all along the length of the flagella of sensitive strains but not on flagella of resistant strains.

Janice Taverne

THOMAS, C. A., Jr. & BERNS, K. I. **The Physical Characterization of DNA Molecules released from T2 and T4 Bacteriophage.** *J. Molecular Biol.* London. 1961, June, v. 3, No. 3, 277–88, 4 figs. [27 refs.]

"The DNA molecules were released from T2 and T4 bacteriophage by a variety of procedures and examined by sedimentation equilibrium in CsCl density gradients and by sedimentation velocity and viscosity. The bands that resulted were quite Gaussian and very narrow, corresponding to molecular weights of about 62×10^6. These samples had sedimentation coefficients of about 57 to 63 s, and intrinsic viscosity values as high as 280 (100 cm^3/g). When these numbers are interpreted in the light of available theories, or empirical calibrations, they are in agreement with the molecular weight values derived from sedimentation equilibrium. The gradient equilibrium method itself has not yet been adequately calibrated in this molecular weight range, and there are certain important doubts concerning the experimental determination of the sedimentation coefficient and the intrinsic viscosity. If these doubts are set aside, it is possible to conclude that there are two molecules of DNA released from each phage particle, each of approximately the same molecular weight, 62×10^6."

BERNS, K. I. & THOMAS, C. A., Jr. **A Study of Single Polynucleotide Chains derived from T2 and T4 Bacteriophage.** *J. Molecular Biol.* London. 1961, June, v. 3, No. 3, 289–300, 9 figs. [11 refs.]

"The phenol-extracted DNA from phage was subjected to various procedures which disrupt the hydrogen bonds, but do not break any of the ester linkages. This denatured DNA reacts rapidly with formaldehyde and, once reacted, there is no tendency to 'renature' or re-establish the former hydrogen bonded structure. These formaldehyde-reacted polynucleotide chains have been examined by density-gradient centrifugation and the band width and band form are compared with the same quantities measured on the undenatured molecules.

"The results indicate that the molecular weight of the single polynucleotide chains is very high, and in no case lower than one-half that of the undenatured molecules from which they are derived. If this is correct, it means that the polynucleotide chains which make up the large undenatured molecules of 62×10^6 mol. wt. consist of only two continuously-linked polynucleotide chains. This conclusion bears on current ideas of genetic recombination."

EGAN, J. B. & HOLLOWAY, B. W. **Genetic Studies on Lysogeny in *Pseudomonas aeruginosa*.** *Australian J. Exper. Biol. & Med. Sci.* 1961, Feb., v. 39, Pt. 1, 9–17, 2 figs. [10 refs.]

"Mutants of the *Pseudomonas aeruginosa* temperate phage D3 have been isolated which are characterised by a clear plaque and a reduced frequency of lysogenisation. They have been classified into three groups on their ability to co-operate in mixed infection to give a lysogenisation frequency characteristic of the wild type. Genetic recombination has been demonstrated for phage D3 and a preliminary linkage map constructed. Crosses between representatives of the three groups of clear plaque mutants confirm the genetic diversity indicated by the co-operation test."

PARNAS, J. Das Phänomen des Bakteriophagenauftretens bei den Stämmen *Brucella brucei*. [**Occurrence of the Bacteriophage Phenomenon in *Brucella* Strains**] *Arch. f. Hyg. u. Bakt.* 1961, May, v. 145, No. 3, 167–83, 6 figs. [34 refs.]

A comprehensive study of the incidence of bacteriophages in *Brucella* strains is based on observations of the author's collection which includes 164 bovine, 28 *melitensis* and 58 *suis* strains as well as a considerable number of atypical strains. The sources of phage have been (a) strains showing phenomena of spontaneous lysis; (b) strains showing unusual appearances (dwarf colonies, etc.) from which phages were obtained by enrichment procedures; and (c) some temperate phages brought out by exposing cultures to ultra-violet light.

The most effective method of those tried for obtaining active phage was to cover 6-month-old cultures on agar slopes with 10 ml. of broth, incubate for 6–10 days and then filter. This method was introduced by DROZEWKINA (in Russia). In all, 48 active phage preparations were obtained and these were specific to *Brucella* strains, but could not be used to differentiate one variety of *Brucella* from another with any regularity, nor did the results indicate any well-defined groups of strains with special patterns of phage sensitivity. *J. W. McLeod*

KOZINSKI, A. W. & UCHIDA, H. **Phage DNA Subunits in the Phage Precursor Pool.** *J. Molecular Biol.* London. 1961, June, v. 3, No. 3, 267–76, 3 figs. [25 refs.]

"In the presence of chloramphenicol, phage precursor nucleic acid (DNA) can be allowed to accumulate to form a large intrabacterial pool, while protein synthesis has been temporarily arrested. Radiophosphorus, ^{32}P, of high specific activity was introduced at various stages and, by following the sensitivity to the radioactive ^{32}P decay of the final progeny population obtained after removal of the antibiotic, the origin of DNA phosphorus of individual phage particles which were derived from the DNA pool has been investigated. The experiments showed that radioactive decay inactivated the great majority of progeny phages, and that DNA synthesized at different points in time appeared together in the same phage individuals. The findings suggest either that the phage DNA is composed of *subunits* which are assembled into the entire viral DNA complement only upon maturation of the phages, or that, if the pool already contains the entire phage DNA complement synthesized in advance of its maturation into protein membranes, *exchange* of homologous subunits of the DNA with each other may occur during their sojourn in the pool."

VIRUSES

The order in this section is:—**General; Psittacosis-Lymphogranuloma group; Pox group; Respiratory group; Reovirus group; Enteric group; Arthropod-borne group; Others.**

LUGINBUHL, R. E.; BLACK, F. L.; HENDERSON, J. R.; HSIUNG, G. D. **Applications of Primary Cell Cultures in the Study of Animal Viruses. I. The Isolation and Characterization of Bovine and Avian Enteric Viruses** [LUGINBUHL & BLACK]. *Yale J. Biol. & Med.* 1961, Apr., v. 33, No. 5, 339–49, 4 figs. (2 on 2 pls.) [31 refs.] **II. Variations in Host Responses to Infection by Certain Arthropod-Borne Viruses** [HENDERSON]. *Ibid.*, 350–58, 6 figs. (5 on 3 pls.) [30 refs.] **III. Biological and Genetic Studies of Enteric Viruses of Man (Enteroviruses)** [HSIUNG]. *Ibid.*, 359–71, 5 figs. (3 on 3 pls.) [43 refs.]

These 3 papers describe various aspects of the use of primary cell cultures as opposed to cell lines in the study of viruses. Such cells are thought to be particularly valuable for isolating viruses.

I. The first paper deals ostensibly with avian and bovine viruses though all the new work deals with bovine viruses. 26 viruses were isolated from 111 faecal specimens. The rate of isolation was higher in younger animals than in older ones, reaching 69% in those 4–11 months old. At least 3 plaque types were seen. The size of 1 type was about 34 millimicrons whereas the other types were a bit bigger. Most of the isolates grew equally well in rhesus monkey and calf kidney cells.

II. In the second paper a pretty comprehensive analysis of the susceptibility of a wide range of cells to 19 arboviruses is described. It was found that 2 cell types—Pekin duck kidney and rhesus monkey kidney—were susceptible to all the viruses used. It was also found that plaque titrations were in general more sensitive to these viruses than fluid cultures or infant mice.

III. In the last paper Hsiung reviews work on the susceptibility of various primate and non-primate cells to enteroviruses. He discusses also factors influencing virus multiplication and in some detail his own work on Coxsackie A9 virus [HSIUNG, this *Bulletin*, 1960, v. 35, 795].

A. J. Beale

SIMINOFF, P. **A Plaque Suppression Method for the Study of Antiviral Compounds.** *Applied Microbiol.* Baltimore. 1961, Jan., v. 9, No. 1, 66–72, 4 figs. [15 refs.]

A method has been developed for the detection of substances with antiviral activity which is based on the suppression of plaque formation in a cell monolayer which has been infected with enough virus to cause confluent cell destruction. 0·5 cc. of a suspension of chick embryo fibroblasts containing about 10^8 cells is mixed with 0·1 cc. of an appropriate dilution of Newcastle disease virus and 2 cc. of nutrient agar; the mixture is then poured over a base layer of nutrient agar in a plate. A sterile filter disc 12·7 mm. in diameter is placed on the surface of the agar, and 0·08 cc. of the solution to be tested is placed on it. The plate is then inverted and kept in a gassed incubator for 72 hours, and then stained with 1:10,000 neutral red solution. If the test solution has antiviral activity the filter disc will be surrounded by a zone in which the cells have been protected against destruction by the virus infection. In tests with vaccinia virus the virus is applied to a monolayer of chick embryo kidney cells, which is then covered with an agar overlay on which the discs are placed. By this method psicofuranine was found to have some activity against vaccinia infection in a concentration of 2–8 mgm. per cc., and β-diethylamino-α-hydroxypropionaldehyde hydrochloride had some activity against Newcastle disease virus in a concentration of 10 mgm. per ml. [A similar method has been described by HERMANN and ROSSELET, this *Bulletin*, 1961, v. 36, 70.] *D. J. Bauer*

TAMM, I., BABLANIAN, R., NEMES, Marjorie M., SHUNK, C. H., FRANKLIN, M., ROBINSON, F. M. & FOLKERS, K. **Relationship between Structure of Benzimidazole Derivatives and Selective Virus Inhibitory Activity. Inhibition of Poliovirus Multiplication and Cytopathic Effects by 2-(α-Hydroxybenzyl)-Benzimidazole, and its 5-Chloro Derivative.** *J. Exper. Med.* 1961, Apr. 1, v. 113, No. 4, 625–56, 9 text figs. & 11 figs. on 3 pls. [25 refs.]

This and the succeeding paper [see below] report very extensive studies, and it is only possible to give some indication of their content and main conclusions. It was predicted by Tamm and his colleagues some years ago that further benzimidazole derivatives could be found with greater virus-inhibiting activity than benzimidazole itself, and this prediction has now been fulfilled, some of the differences in activity exceeding 100-fold.

There were 2 series of experiments. In the first, 65 benzimidazole, naphthimidazole and benzotriazole derivatives were examined for activity against influenza virus B in the chorioallantoic membrane. A table occupying 8 pages gives the structure of each compound, the concentration causing 75% inhibition of virus growth, that producing a certain degree of tissue damage to the embryo, and hence the selectivity ratio. These findings enable the relation of structure to biological activity to be examined at considerable length. Secondly, 19 benzimidazole and 6 benzotriazole derivatives were tested for capacity to inhibit the growth of poliovirus type 2 in monkey kidney tissue cultures, observations again being made also on the effect on the tissue itself. These included 5 compounds highly active against influenza virus B: these also showed high activity against poliovirus, but they also possessed a high tissue toxicity. On the other hand 2-(α-hydroxybenzyl)-benzimidazole (HBB) and its 5-chloro derivative, although without action on influenza virus, were highly inhibitory to poliovirus and had a relatively low tissue toxicity (selectivity ratios given as

>31 and >29). The effect of different concentrations of these substances on both virus and tissue were examined quantitatively and are represented graphically.

L. P. Garrod

EGGERS, H. J. & TAMM, I. **Spectrum and Characteristics of the Virus Inhibitory Action of 2-(α-Hydroxybenzyl)-Benzimidazole.** *J. Exper. Med.* 1961, Apr. 1, v. 113, No. 4, 657–82, 11 text figs. & 6 figs. on pl. [27 refs.]

This paper is concerned solely with the action of HBB (see previous paper above). It was found to inhibit the growth only of certain enteroviruses: these were the 3 types of poliovirus, 7 types of Coxsackie (5 others were unaffected), and 24 types of ECHO virus (3 others unaffected). Others unaffected were arbor, reo and adenoviruses, influenza B, para-influenza, mumps, herpes simplex and vaccinia. Action on all these viruses is represented by graphs of percentages of cells showing virus-induced damage against time for 2 or 3 concentrations of HBB. Exposure to HBB sometimes resulted in reduced virus-susceptibility to it. HBB does not reduce virus infectivity, but appears to interfere in some way with intracellular virus multiplication. It did not alter the morphology of the cells, nor was any action demonstrable on their oxygen uptake, glucose utilization, lactic acid production, incorporation of adenosine into RNA, or alanine into proteins. *L. P. Garrod*

ANDREWS, R. D. **Specificity of Interferon.** *Brit. Med. J.* 1961, June 17, 1728–30, 2 figs. [12 refs.]

Interferons prepared in cells from chick embryos, rabbits, calves and monkeys were tested in rabbits and a monkey for their ability to modify the lesions produced by intradermal inoculations of vaccinia virus. When given 24 hours before challenge with vaccinia virus, most of the interferons prevented necrosis or reduced the diameter of the lesion, or both. When given at the same time as the vaccinia virus, rabbit and monkey interferon were more effective than chick interferon. In the monkey, one chick preparation completely inhibited the development of the vaccinial lesion, the other had no effect. Rabbit interferon was also ineffective. Interferon from rhesus monkey cells was moderately effective in cynomolgus monkey skin, while cynomologus interferon was completely effective.

Athough homologous interferons do have an advantage, heterologous preparations may nevertheless be useful. *Colin Kaplan*

HITCHCOCK, Griselda & PORTERFIELD, J. S. **The Production of Interferon in Brains of Mice infected with an Arthropod-Borne Virus.** *Virology.* New York. 1961, Mar., v. 13, No. 3, 363–5, 2 figs.

Mice 36 days old were infected intracerebrally with about 300 plaque forming units (PFU) of the 6th infant mouse passage of the Osege strain of O'nyong-nyong virus, and groups were killed daily. The brains were titrated on chick embryo cultures and brain extracts were prepared by dialysis at *p*H 2 to eliminate infectivity, then centrifuged. The interfering activity of the brain extracts was titrated against encephalomyocarditis virus (EMC) on secondary mouse embryo fibroblast cultures. 2 days after infection there was marked protection by brain extracts and this was more marked 4 days after infection. The virus titre of the brains was maximal (about 10^4 PFU/ml.) 48 hours after infection and fell steadily thereafter to about 10^2 in the 7th day after infection. The percentage protection afforded by brain extracts against 50–100 plaques of EMC rose from about 20% 24 hours after infection to a maximum of 80% on the 4th day, after which it remained between 60 and 80% up to 7 days.

The interfering material was not removed by centrifugation of brain extracts at 100,000 g for 4 hours. Its activity was unaffected if O'nyong-nyong immune serum was incorporated in the overlay of the EMC titration. The extracts had no activity against Semliki Forest virus in chick embryo cultures. The properties of the interfering agent are thus consistent with its being interferon. O'nyong-nyong virus multiplies in the brains of adult mice but does not kill them and it is suggested that this is because of interferon production. Adaptation to adult mice might be more readily achieved if brains were passaged after 48 hours when infectivity is maximal and interferon has not yet reached its peak.

C. E. Gordon Smith

WAGNER, R. R. **Biological Studies of Interferon. I. Suppression of Cellular Infection with Eastern Equine Encephalomyelitis Virus.** *Virology.* New York. 1961, Mar., v. 13, No. 3, 323–37, 5 figs. [22 refs.]

Allantoic fluid infected with WS(E) influenza A virus was added to chick embryo cultures. After absorption for 1 hour, the cultures were washed and dilutions of eastern encephalitis (EE) virus added. Fluid containing $10^{9.5}$ ID50 of WS interfered with 10^9 PFU (plaque-forming units) of EE but a dilution containing $10^{7.5}$ ID50 failed to interfere even with 3 PFU. Infected allantoic fluid was repeatedly centrifuged (42,000 g) to remove infectivity: removal of 99·999% of infectivity did not reduce the interfering power of the fluid. The infectivity was reduced another 100-fold by absorption with erythrocytes and interference was still unaffected. The sedimented infectious virus also interfered but destruction of the infectivity by heating at 65° C. for 1 hour destroyed interference while the interfering power of the supernatant was unaffected by heating.

In subsequent experiments interferon was prepared by 3–4 1-hour cycles of centrifugation at 100,000 g and assayed by mixing 2-fold dilutions with about 100 PFU of EE, plating the mixtures and overlaying after 1 hour without washing. Prior incubation of the interferon on the cells was found unnecessary if the cultures were not washed. 256 units of interferon were incubated with about 10^7 PFU of EE, the mixture was diluted and plated. Interference was found only within the dilution titre of the interferon and the endpoints were similar. This was confirmed by mouse titration. Interferon was absorbed rapidly to chick embryo cells during the first 20

minutes of incubation but more slowly thereafter. The smaller the volume plated, the more rapid the absorption. Effectiveness of interferon depended therefore on both dose and time of contact with cells. Cells grown for 24 hours in the presence of interferon were dispersed and washed: 48 hours later they were still resistant to plaque formation by EE. EE virus absorbed as rapidly to interferon-treated cells as to normal cells.

The yields of virus in single cycles of multiplication were studied after interferon treatment: control cells yielded about 5,000 PFU per cell compared with only 20 per cell when interferon was added with the inoculum and only 1–2 per cell when the interferon was added 12–48 hours before; the latent period also appeared to be prolonged. When interferon was added 1 hour after the virus the yield was about 5 PFU per cell. There was still some reduction in yield when interferon was added 2 and 4 hours after the virus although the multiplicity of the inoculum was about 5 PFU per cell. Interferon heated to remove residual infectivity was used to pretreat chick embryos before infection with EE: treated embryos gave an endpoint titre by mortality of $10^{4\cdot6}$ compared with $10^{5\cdot8}$ for controls. In treated eggs infected with 500 LD50 of EE the mean time of death was 43·5 hours compared with $28\cdot6 \pm 2\cdot68$ hours for controls. Interferon prepared in duck embryos was compared with chick-embryo interferon in cultures of chick and duck embryo cells. Duck interferon was inferior in titre but host specificity of activity was demonstrated for both duck and chick embryo. *C. E. Gordon Smith*

GREENLAND, Rima M. & MOULDER, J. W. **A Search for Genetic Interaction in the Psittacosis Group.** *J. Infect. Dis.* 1961, May-June, v. 108, No. 3, 293–303, 1 fig. [38 refs.]

Four members of the psittacine group with double drug resistance as genetic markers—penicillin-and-sulphadiazine-resistant psittacosis and feline pneumonitis viruses, and chlortetracycline-and quinoxaline-oxide-resistant psittacosis and feline pneumonitis viruses—were used in this investigation. Infection of the chick embryo by the yolk sac and chorio-allantoic routes were made with suitable pairs of these 4 strains, a heavy inoculum being used so as to ensure a high incidence of doubly infected cells. Passage in the presence of appropriate combinations of drugs was done to enrich the growth in possible recombinants, and clones were obtained from the resulting populations by passage in the yolk sac at limiting dilutions. These were then tested for resistance to the 4 drugs. 57 clones from 11 different crosses were examined and none showed any evidence of genetic transfer. The authors point out that this negative finding does not prove that no genetic interaction occurred.

S. P. Bedson

FAGRAEUS, Astrid & ESPMARK, A. **Use of a "Mixed Haemadsorption" Method in Virus-Infected Tissue Cultures.** [Correspondence.] *Nature.* 1961, Apr. 22, v. 190, 370–71, 1 fig.

Tissue cultures infected with vaccinia virus and with measles and canine distemper viruses were treated with virus-specific antisera prepared in either rats or rabbits. Sheep red cells were then coated with either anti-rat or anti-rabbit sera and added to thrice-washed tissue cultures. In infected cultures coated red cells were adsorbed to the surfaces of infected culture cells, while uncoated red cells were not. In uninfected control cultures tests were negative. Two methods are described of attaching and treating red cells, one involving tanned cells and the other not.

At the time of publication this method had not been successful in demonstrating infection with poliomyelitis and herpes simplex viruses. *Colin Kaplan*

BAUER, D. J. **The Zero Effect Dose (E_0) as an Absolute Numerical Index of Antiviral Chemotherapeutic Activity in the Pox Virus Group.** *Brit. J. Exper. Path.* 1961, June, v. 42, No. 3, 201–6, 3 figs.

"The response of mice infected with neurovaccinia virus to treatment with isatin β-thiosemicarbazone bears a linear relation to the logarithm of the dose of compound administered. The point of intersection of this dose-response line with the value of the response obtained in untreated mice represents the dose at which no chemotherapeutic effect is obtained. This value is termed the zero effect dose, or E_0, and was found to be independent of the dose of virus used for infection. The value of E_0 therefore characterizes the chemotherapeutic effect of isatin β-thiosemicarbazone in absolute numerical terms without relation to an arbitrary standard of activity. Dose-response curves of anti-viral effect were also obtained with rabbitpox, cowpox and white cowpox viruses, and were similarly independent of the virus dose. The values of E_0 thus obtained enabled a comparison to be made of the chemotherapeutic activity of the same compound against different viruses. The order of sensitivity of the viruses was as follows: ectromelia $\leqslant$ cowpox $<$ white cowpox $<$ neurovaccinia $<$ rabbitpox. The implications of the concept of the zero effect dose upon the planning of antiviral chemotherapy and upon virus genetics are pointed out."

[The findings suggest that the activity of isatin β-thiosemicarbazone is directed against the virus, rather than the intracellular replicating mechanism, since all the viruses used are presumably genetically related and should use at least some of the same intracellular pathways. And as there seems to be a spectrum of sensitivity to the drug the author is doubtful whether a formal approach to the genetics of pox viruses is *à propos* since analysis of other markers such as heat resistance may show a similar shading of sensitivities from one virus to another.] *Colin Kaplan*

COCCHI, P. **Antiviral Activity of 4-Aminopteroylglutamic Acid on Vaccinia Virus in Tissue Cultures.** *Antibiotics & Chemotherapy.* New York. 1961, Feb., v. 11, No. 2, 79–88, 4 figs. [14 refs.]

This paper from the Institute of Infectious Diseases, University of Florence, reports that very low concentrations of 4-aminopteroylglutamic acid (aminopterin) prevent the growth of vaccinia virus in tissue cultures of

human embryonic epithelium. Several antibiotics and colchicine derivatives had no effect. The inhibitory concentration of aminopterin varied with the size of the virus inoculum. The presence of folic acid in equivalent amounts did not interfere with the action of aminopterin.

L. P. Garrod

CAUNT, Anne E., RONDLE, C. J. M. & DOWNIE, A. W. **The Soluble Antigens of Varicella-Zoster Virus produced in Tissue Culture.** *J. Hygiene.* 1961, June, v. 59, No. 2, 249–58. [12 refs.]

Human amnion cells infected with zoster or chickenpox viruses produced usable concentrations of complement-fixing antigen when incubated at 36°–38°C. in a medium consisting of equal volumes of bovine amniotic fluid and Hanks's solution. The culture fluids had to be concentrated 5- to 20-fold for complement-fixation tests: this was done by freeze drying after removal of salts by dialysis. Tests with these antigens gave results comparable with those given by good vesicle fluids.

Colin Kaplan

HINZE, H. C. & WALKER, D. L. **Occurrence of Focal Three-Dimensional Proliferation in Cultured Human Cells after Prolonged Infection with Herpes Simplex Virus.** *J. Exper. Med.* 1961, May 1, v. 113, No. 5, 885–98, 1 text fig. & 3 figs. on pl. [13 refs.]

A culture of human conjunctival cells (Chang) after prolonged infection with the HF strain of herpes simplex virus started, here and there, to grow upwards away from the glass, producing masses 15 to 20 cell layers thick. Between the proliferating foci the cells grew as an ordinary monolayer. This C4 cell line did not grow faster than the parent cells. It was not composed of a mixed population of cells as no clones derived from it grew exclusively as a monolayer but always showed the new growth pattern of thickened foci and intermediate monolayer. This growth pattern only occurred when the culture medium contained human serum, but it did not depend upon the presence of herpes antibody. When horse serum was substituted the cells grew in a monolayer, broken by focal areas of degeneration consisting of cells with pyknotic nuclei, which did not however make holes in the cell sheet.

The growth pattern described was never observed in conjunctival cell cultures which had not been infected with herpes virus. The phenomenon occurred only once, and then in a culture which had been infected and held at 30°C. for 10 weeks. (It also occurred once in a culture of KB human carcinoma cells growing in similar conditions.) Although initially herpes antibody was present in human serum in the culture medium, the phenomenon could not be induced by growing infected cultures in the presence of rabbit immune serum. The cell change appeared to be induced by herpes infection, but at no time could virus be isolated from the cells. No herpes antigen could be detected by complement-fixation or by staining with fluorescent antibody and the release of virus was not induced by exposing the cells to UV light or X-rays. The cells were in fact as susceptible to infection by herpes as was the parent cell line, and they showed the same sensitivity to other viruses.

The authors consider that the phenomenon results from a stable, heritable change in the cells brought about by the virus. They compare it with the proliferative changes described in cultures infected with Rous sarcoma virus which were apparently free of virus (PRINCE, *Virology*, 1960, v. 11, 400) and with changes occurring in cells infected with polyoma virus which depended on the composition of the medium and which were accompanied by reduced virus production (VOGT and DULBECCO, *Proc. Nat. Acad. Sci.*, 1960, v. 46, 365). *Janice Taverne*

VEERARAGHAVAN, N. **Influenza Virus Isolations at the Government of India Influenza Centre, Coonoor, during 1950–60.** *Bull. World Health Organization.* Geneva. 1961, v. 24, No. 6, 679–86.

VEERARAGHAVAN, N. & KIRTIKAR, M. W. **Biological Characteristics of Influenza Virus Strains isolated at the Government of India Influenza Centre, Coonoor, during 1950–60.** *Bull. World Health Organization.* Geneva. 1961, v. 24, No. 6, 687–93.

HAMRE, Dorothy, LOOSLI, C. G. & EWERT, R. C. **Antigenic Variants of Influenza A Virus (PR8 Strain). VI. Results of Repeated Passages of the Same Variant in Mice Immunized with Monovalent Homologous Vaccine or Polyvalent Vaccine.** *J. Infect. Dis.* 1961, Mar.–Apr., v. 108, No. 2, 151–62, 5 figs.

Previous papers in this series have reported the isolation of antigenic variants of the PR8 strain of influenza virus from mice infected with the parent strain after homologous immunization. In the present report, one such variant, DC, was passed 4 times serially through mice which had been immunized with DC vaccine. 4 completely new antigenic variant virus strains were recovered from the mice during this process. All these strains contained new predominant antigens in addition to some shared with previous variants of the PR8 strain.

In a further attempt to determine the degree of antigenic suppression or antigenic variation resulting from animal infection in the presence of antibody, the strain DC was passaged serially through mice immunized with a vaccine containing both DC and original PR8 virus. All the viruses recovered from such mice were identical with each other and with one of the variants from the DC-vaccinated animals. These variants continued to possess PR8 antigen despite their growth in mice with circulating antibody to PR8 strain. *D. Hobson*

FREDERIKSEN, H. **Epidemiological Significance of the Interference Phenomenon.** *Amer. J. Trop. Med. & Hyg.* 1961, Mar., v. 10, No. 2, 271–2.

"Immune reactions to influenza A and B are so different that the prevalence of one type of influenza

would not be influenced by immunity to the other type, and yet a negative correlation between the natural distributions of influenza A and B becomes apparent in the compilation of influenza virus isolations in the United States by year since 1948.

"The observation of a negative correlation between the distributions of influenza A and B viruses seems to be inexplicable on the basis of hitherto accepted epidemiological principles. This suggests consideration of interference as an epidemiological factor in the natural distribution of viruses which display interference under experimental conditions. Such a working hypothesis would seem to be consistent with experimental and epidemiological observations and may prove to be tenable at least as long as the negative correlation between natural distributions of interfering viruses continues to hold."

COHEN, A. & BELYAVIN, G. **The Influenza Virus Hemagglutination Inhibitors of Normal Rabbit Serum. I. Separation of the Inhibitory Components.** *Virology.* New York. 1961, Jan., v. 13, No. 1, 58–67, 4 figs. [26 refs.]

To establish the chemical identity of the α, β and γ inhibitory components of normal rabbit serum it was necessary to define the serum fractions in which they were contained. The serum was separated into euglobulin and pseudoglobulin fractions by precipitation with ammonium sulphate and protein remaining soluble at 50% saturation was termed the "albumin" fraction. The euglobulin fraction was further separated into water-soluble and -insoluble components by dialysis against distilled water. Then the serum components present in each fraction were identified by paper electrophoresis; 2 electrophoretic components, albumin and β-globulin were identifiable in the "albumin" fraction and the water-soluble and -insoluble euglobulins consisted wholly of γ-globulin with part of the latter and the α-globulin in the pseudoglobulin fraction, with, in some experiments, a faint β-globulin band.

The distribution of inhibitory activity among the fractions was determined in haemagglutination-inhibition tests against the following strains:—ASH, an A-prime strain for the detection of β-inhibitor; ROB, a B strain, used after heating at 56°C. for 30 minutes, for the detection of α activity and an A2 (Asian) influenza strain. In addition, fractions treated with receptor-destroying enzyme (RDE) and controls subjected to the same thermal conditions were titrated in parallel. Any activity recovered in the water-soluble euglobulin fraction was α in type. The water-insoluble euglobulin fraction possessed both α and γ inhibitory activity and also some β inhibitor. The γ inhibitor was distinguished by its activity against the A2 strain and its partial sensitivity to RDE. The pseudo-globulin fraction contained about half the α inhibitory activity and β inhibitor was present in greatest amount in this fraction. The albumin fraction contained α-type inhibitor only. Thus, in conclusion, the α inhibitor was present in all the serum fractions and the γ inhibitor in the γ-globulin fractions. [See also KRIZANOVÁ-LAUCÍKOVÁ, *et al.*, this *Bulletin*, 1961, v. 36, 499.]

D. Taylor-Robinson

SPRINGER, G. F. & STALDER, K. **Action of Influenza Viruses, Receptor-Destroying Enzyme and Proteases on Blood Group Agglutinogen *Mg*.** [Correspondence.] *Nature.* 1961, July 8, v. 191, 187–8. [11 refs.]

ÔSATO, T. & ISHIDA, N. **The Development of Sendai Virus in Earle's L Cells as revealed by Fluorescent Antibody Staining. Growth Characteristics of Myxoviruses in Tissue Culture. Fourth Report** *Tohoku J. Exper. Med.* 1961, Feb. 25, v. 73, No. 3, 201–14, 20 figs. (6 coloured) on 3 pls. & 1 chart. [14 refs.]

Following their earlier studies on the adsorption and growth of Sendai virus in L cells [this *Bulletin*, 1961, v. 36, 814], the authors stained infected cells using rabbit antiserum with a high anti-haemagglutinin titre (5120 in HI test) and a goat anti-rabbit serum conjugated with fluorescein. 1–2 hours after adding egg-passed Sendai virus (80 EID50/cell) specific fluorescence was seen on the cell surface which faded until 4 hours when it appeared in the cytoplasm near the nucleus and adjacent to the Golgi zone. The concentration increased and then scattered to the periphery of the cells from 16–18 hours. At 24 hours the cytoplasm broke down and "jagged fluorescence" was seen. When they used virus passed in L cells antigen could be seen absorbed to the cell surface but no new formed antigen was detected.

D. A. J. Tyrrell

HOMMA, M. **A Particular Binding of L Cell-Grown Sendai Virus by Host L Cells. (Growth Characteristics of Myxoviruses in Tissue Culture, 5th Report.)** *Tohoku J. Exper. Med.* 1961, Feb. 25, v. 73, No. 3, 215–29, 4 figs. [16 refs.]

Further studies are presented of the Sendai virus (L-Var) grown in L cells; this virus will infect chick embryo but not L cells. As measured by haemagglutination it is absorbed to L cells to the same extent as is normal egg-grown virus (E.-Orig.). The L-Var virus induces interference against E.-Orig. virus if added before or within one hour of the addition of the latter. No interferon could be detected when medium and extracts of cells in a state of interference were tested in L cells with the same challenge virus—E.-Orig. Both viruses eluted from L cells but 76% of L-Var eluted in 80 minutes at 37°C. compared with 20% of E.-Orig. Both viruses destroyed the non-specific inhibitor of mouse lung. L cells treated with L-Var virus for 1 hour showed no interference if they were then treated with antibody—after 16 hours antibody had no effect. Sucrose density gradient fractionation showed that L-Var contained a less dense fraction as well as one of a similar density to E.-Orig. Both fractions failed to infect L Cells. The author says in discussion that he has obtained variants similar to L-Var on inoculating into HeLa cells HA2 virus which had been propagated in monkey kidney cells.

D. A. J. Tyrrell

BELLELLI, E., VITALI, M. A. & MONACI, V. Sulla tipizzazione degli adenovirus con la prova di I.E.A. **[The Typing of Adenoviruses by the Haemagglutination-Inhibition Test]** *Ann. Sclavo.* Siena. 1961, Mar.–Apr., v. 3, No. 2, 161–70. English summary.

The authors studied haemagglutination and haemagglutination-inhibition tests in their relation to the neutralization tests. Haemagglutination tests were made on 18 prototype adenoviruses, haemagglutination-inhibition tests on 9 prototypes with the relative immune sera, and also comparative typing tests with haemagglutination-inhibition and neutralization in tissue culture of recently isolated strains.

Types 3, 7, 11, 14 and 16 were found to agglutinate *Macacus rhesus* red cells, types 9, 10, 15 and 17 agglutinated rat red cells, while types 2, 4, 5, 6, 8, and 12 only agglutinated the cells of individual rats; types 1, 13, and 18 did not agglutinate either rat or rhesus cells.

Haemagglutination-inhibition tests on 9 prototypes proved the specificity of the reaction.

26 strains which agglutinated rhesus cells were tested by haemagglutination-inhibition and by neutralization tests, which were found to match completely (5 of type 3, 21 of type 7). In 47 strains which agglutinated rhesus cells both haemagglutination and neutralization tests gave the same results. 17 strains which agglutinated rat cells were found by neutralization tests to belong to groups 2, 4, 5, and 6, while 15 which did not agglutinate either rhesus or rat cells were found to belong to types 1, 2, and 5.

The authors consider haemagglutination a useful screening test, saving time and reagents. They note, however, that certain strains of adenoviruses may not produce agglutinin on first isolation. *E. Agius*

DOSSENA, G. Coltura degli adenovirus su cellule umane ed animali. **[Cultivation of Adenoviruses on Human and Animal Cells]** *Ann. Sclavo.* Siena. 1961, Mar.–Apr., v. 3, No. 2, 171–7. [12 refs.] English summary (8 lines).

This reports an investigation into the power of kidney cells of various animals to grow various types of adenoviruses, culture on KB and HeLa cells being used as a control.

Primary explants of kidney cells of various animals were obtained by trypsinization of the tissue by YOUNGNER'S method [this *Bulletin*, 1954, v. 29, 1005]. They were cultivated in lactalbumin hydrolysate in Hanks solution with 2% calf serum and maintained in lactalbumin hydrolysate in Earle's solution without serum. Kidney cells from *Macacus rhesus*, hamadryad monkey, calf, swine, dog, cat, rabbit, guineapig, and mouse were used, besides embryonic cells from chicken lung; 17 types of human adenoviruses previously kept on KB and HeLa cells were tested. Cultures with a continuous cell layer were seeded with 0·2 ml. of whole viral liquid and with 10-fold dilutions, 5 tubes being used for each type of virus and for each dilution. Cultures were kept at 36°C. in a rotating drum for 6 to 8 days. A transmissible cytopathic effect was taken as the criterion for adaptation and multiplication of the virus.

All the 17 types multiplied producing the typical cytopathic effect on calf, *M. rhesus*, hamadryad monkey and rabbit; 15 adapted to swine cells; 12 to dog, guineapig and cat cells; 13 to embryo chicken lung cells, while only 10 did so to mouse cells. Adenoviruses adapt themselves more easily than the enteroviruses of which only ECHO 10 and Coxsackie B3, B4 and B5 have shown adaptability to kidney cells from various animals [this *Bulletin*, 1961, v. 36, 302]. *E. Agius*

DOSSENA, G. Resistenza degli adenovirus tipo 1, 2, 5 e 6 a varie temperature. **[Resistance of Adenoviruses type 1, 2, 5 and 6 to Various Temperatures]** *Ann. Sclavo.* Siena. 1961, Mar.–Apr., v. 3, No. 2, 178–83. English summary (6 lines).

This note describes the effect on adenoviruses 1, 2, 5, and 6 of temperatures of −20°, 4°, 20°, and 36°C. for periods ranging from 5 days to 6 months at *p*H about 7. The viruses were kept on trypsinized monkey kidney cells and on KB cells. Culture was made on lactalbumin hydrolysate in Hanks solution with 2% ox serum added in the case of the kidney cells and 5% for the KB cells. KB cells were maintained in the same medium without serum, while the kidney cells were kept in lactalbumin hydrolysate in Earle's solution without serum. The viral suspensions were obtained by centrifugation of 2–4 day cultures on KB cells, the supernatant being preserved in sealed tubes kept in the refrigerator at −20°C., in the ice-box at 4°C., at room temperature (20°C.), and in the incubator at 36°C. Survival was estimated by seeding 0·2 ml. of virus at varying dilutions.

At 36°C. the 4 types showed good survival after 5 days which decreased after 30 days, with no survival at 90. A similar result occurred at 20°C., but there was still some survival at 90 days with complete disappearance at 180 days. At 4°C. the viruses survived at least up to 180 days. At −20°C. the infective titre was still fairly high 6 months later.

These points have a practical bearing on examination of pathological materials. In the author's laboratory 21 faeces samples which had shown the presence of adenoviruses when first received gave positive results after 12 months at −20°C. These survival powers can also have a bearing on the epidemic spread.

[See also this *Bulletin*, 1957, v. 32, 211.] *E. Agius*

TINT, H. & STONE, J. **An Adenovirus Vaccine Potency Test.** *J. Immunology.* 1961, Mar., v. 86, No. 3, 253–6.

Formaldehyde-inactivated adenovirus vaccines types 3, 4 and 7 were mixed with mineral oil adjuvant and inoculated intramuscularly into guineapigs. The animals were bled before inoculation and 21 to 28 days after, and the sera were titrated for neutralizing antibody. The mean antibody level of a group of guineapigs was used as a measure of the potency of the antigen and was expressed as a " potency ratio " by comparing the geometric mean

titre with that produced by NIH reference vaccine. A drop in "potency ratio" was shown after storing a trivalent vaccine at 37°C. for 4 weeks. The vaccines used induced antibody formation when diluted 10^{-2} and given intraperitoneally in 1 ml. volumes 3 times at weekly intervals. This method and the antigen extinction assay will be tested against "efficacy . . . in the field".

[It is unlikely that the "potency ratio" described measures at all accurately the difference between the antigenic activity of different vaccines and there is no experiment on this point.] *D. A. J. Tyrrell*

CHOPPIN, P. W. & PHILIPSON, L. **The Inactivation of Enterovirus Infectivity by the Sulfhydryl Reagent *p*-Chloromercuribenzoate.** *J. Exper. Med.* 1961, Apr. 1, v. 113, No. 4, 713–34, 6 figs. [29 refs.]

These authors have previously shown that certain sulphydryl reagents including *p*-chloromercuribenzoate (PCMB) neutralize the haemagglutinating activity of enteroviruses. This paper reports an extension of this study, first to virus infectivity in tissue cultures. That of ECHO 7 and Coxsackie B3 viruses was greatly reduced by PCMB, and that of ECHO 9 and poliovirus 2 to lesser degrees. This reaction was found to be affected to different degrees in 4 different buffers, being least in a barbital and most in a phosphate buffer. Infectivity could be restored by adding reduced glutathione. Evidence was also obtained that PCMB interferes with or renders unstable adsorption of ECHO 7 virus to monolayer cultures of monkey kidney cells. On the other hand, although abolishing infectivity of influenza viruses, it did not prevent adsorption of these viruses to the chorioallantoic membrane. It is concluded that sulphydryl groups in enteroviruses "are involved in the establishment of infection, and that they play a role in the adsorption of virus to host cells". *L. P. Garrod*

DAGUET, G. L., ROGER, F. & ROGER, Annie. La technique de séro-identification rapide des virus poliomyélitiques dans les selles. I. Partie pratique. **[Technique of Rapid Sero-Identification of Polioviruses in Stools. I. Practical Studies]** *Ann. Inst. Pasteur.* 1961, May, v. 100, No. 5, 656–71, 1 fig. [15 refs.]

An interesting technique for the rapid identification and isolation of polioviruses is described. Stools are extracted and clarified by 2 cycles of slow-speed centrifugation. Stool suspension is then added to 15 Kahn tubes in batches of 3 (without serum, with the 3 poliovirus antisera separately, and a pool of the 3 sera). KB cells and liquid paraffin are added after 3 hours at 37°C. The tubes are examined daily with an inverted microscope. In this way a serological typing can be achieved in 3 days on the average.

In a study of 54 patients, 23 yielded a virus typed by this technique and 23 out of 53 studied serologically were diagnosed as poliovirus infections. In addition the serum neutralization test [this *Bulletin*, 1960, v. 35, 93] allowed 10 cases to be excluded from consideration as poliovirus infections. A combination of both methods is recommended.

[Full technical details are given.] *A. J. Beale*

SU, Chan-Tsing. **Use of the Colour Test for Virological Investigations in Poliomyelitis.** *Problems of Virology.* London. 1960, v. 5, No. 4, 430–36. [19 refs.] [Translated from Russian.]

The metabolic inhibition test of SALK *et al.* [this *Bulletin*, 1955, v. 30, 184] has been extensively used for the titration of antibodies to poliovirus and to a lesser extent to titrate virus. The author describes the value of the method for the isolation, titration and typing of strains of poliovirus from faeces. He found that the test was very satisfactory for the epidemiological control of vaccination programmes with Sabin's type 1 attenuated poliovirus. The results obtained were in close agreement with those obtained by observing cytopathic effects in established monolayers although the titres were somewhat lower. Approximately 5% of the faecal extracts were toxic to cells or gave non-specific cell destruction. All 3 types of poliovirus were satisfactorily isolated, titrated and typed. The cells used were either 2nd generation monkey kidney or a continuous cell line, SOT, derived from a cynomolgus monkey heart. *A. J. Beale*

MAYOR, Heather D. & DIWAN, A. R. **Studies on the Acridine Orange Staining of Two Purified RNA Viruses: Poliovirus and Tobacco Mosaic Virus.** *Virology.* New York. 1961, May, v. 14, No. 1, 74–82. [23 refs.]

ANDERSON *et al.* have shown that the acridine orange fluorescent staining technique for DNA and RNA is a powerful tool for examining viruses (*9th Symposium Soc. Gen. Microbiol.*, 1959, 224). This stain under standard conditions gives a brilliant flame red with RNA and bright apple green fluorescence with DNA. In this paper the results of staining purified concentrated tobacco mosaic virus [TMV] and type 1 poliovirus and the results of experiments on growing poliovirus in cultures containing acridine orange are described. It was found that TMV virus stained brilliant apple green when unfixed and flame red after fixation with Carnoy's fluid or 70–100% methanol. Unfixed poliovirus did not stain but after fixation flame red fluorescence was produced. The incorporation of acridine orange into growing poliovirus resulted in apple green fluorescence and a similar colour was produced when fixed concentrates were stained with a low concentration of dye. In the incorporation experiments, owing to the toxicity of the dye for cells even in the dark, only very low concentrations could be used. The authors calculated that the acridine orange technique is sufficiently sensitive to visualize about 50 close-packed virus particles. RNase treatment destroyed or reduced the capacity of virus to fluoresce when stained with acridine orange.

[The details of the fluorescence microscopy are given by MAYOR, *Texas Reports Biol. & Med.*, 1961, v. 19, 106.] *A. J. Beale*

DARNELL, J. E., Jr., LEVINTOW, L., THORÉN, Marilyn M. & HOOPER, J. L. **The Time Course of Synthesis of Poliovirus RNA.** *Virology.* New York. 1961, Mar., v. 13, No. 3, 271–9, 3 figs. [28 refs.]

The time of synthesis of viral RNA in HeLa cells infected with poliovirus was determined by 2 independent methods. (a) The incorporation of a radioactive label from a precursor added at various intervals to the cells. This method had previously been successfully used for following virus protein synthesis (DARNELL and LEVINTOW, *J. Biol. Chem.*, 1960, v. 235, 74) but lacked precision owing to variations in the amount of radioactivity of the added adenosine reaching the nucleic acid precursor pool. (b) The isolation of infectious RNA. This was done by 2 methods which gave similar results. It was found that poliovirus RNA appeared between 2 and 3 hours after infection (2 hours was the time of the first increment in infectious RNA) and thereafter increased rapidly to completion at 6 hours. The time course of viral RNA and protein development was closely similar. This finding is at variance with studies on other viruses where nucleic acid synthesis precedes virus maturation, *e.g.*, vaccinia [SALZMAN, *Virology*, 1960, v. 10, 150; this *Bulletin*, 1960, v. 35, (510)], encephalomyocarditis virus [SANDERS, *ibid.*, 1060] and foot and mouth disease virus (BROWN and STEWART, *Virology*, 1959, v. 7, 408). *A. J. Beale*

SERGIESCO, Dina, KLEIN, R. & HORODNICEANU, F. **Character of Plaque Formation by Polioviruses in Various Common Cell Culture Systems.** *Arch. Roumaines Path. Expér. et Microbiol.* 1961, Mar., v. 20, No. 1, 115–27, 4 figs. [47 refs.]

This paper contains a detailed account of the plaque method of titration of polioviruses, with 4 cell types: (1) Primary rhesus monkey kidney cells, (2) first passage rhesus monkey kidney cells, (3) HeLa cells, (4) Detroit 6 cells. HeLa cells were found to give lower titres and inferior plaques. Either primary or first passage monkey kidney cells were as good as Detroit 6 cells, but the latter were preferred because of their ready availability. In these experiments it was found that slightly higher titres of infectious units were obtained in tube titrations than in plaque titrations with the Mahoney, MEF1 and Saukett strains of polioviruses 1, 2 and 3, respectively. Titres were slightly higher by the plaque technique, as has been described in the literature, using the Brunenders strain of type 1 poliovirus. *A. J Beale*

TAKAHASHI, M., YAMAMURA, T., TOYOSHIMA, K., MIKI, T. & OKUNO, Y. **Studies on Attenuation of Poliovirus. I. Serial Cultivation of Poliovirus (Type 1, Brunhilde Strain) in developing Chick Embryos.** *Biken's J.* Osaka. 1960, Oct., v. 3, No. 3, 249–57.

Attempts were made to adapt type 1 poliovirus (Brunhilde strain) to chick embryos. 9 passages were made by inoculating virus and HeLa or FL cells onto the chorioallantoic membrane [CAM] and then 9 passages were made of virus only (as CAM extract in allantoic fluid) on the chorioallantoic membrane. Thereafter virus wa passed in the allanotic cavity. The presence of virus wa assessed by its interference with the production o haemagglutinin of mumps virus inoculated into the allan toic fluid. With this method of detecting virus it wa found that the virus still interfered with mumps viru at a dilution of over 10^{-5} at the 8th, 25th and 28t passages in eggs. The virus was considered to be polio virus despite the fact that after the 9th passage it n longer caused cytopathic effects in FL or monkey kidne cells because: (1) no inhibition of mumps virus occurre after treatment with poliovirus-immune serum; (2) the virus produced paralysis and histological evidence o poliomyelitis in monkeys inoculated intraspinally; (3 monkeys given the virus were protected against a type poliovirus strain (Brunhilde) given orally. 1 contro monkey was paralysed. 5 vaccinated monkeys (3 orally 2 intramuscularly) were protected. *A. J. Beale*

SHAND, F. L. **A Modified Colour Test Technique for the Estimation of Poliovirus Neutralising Antibody.** *J. Med. Lab. Technol.* 1961, Apr., v. 18 No. 2, 75–82, 3 figs.

This paper describes 4 separate things. First, a modification of the metabolic inhibition test of SALK *et al.* [this *Bulletin*, 1955, v. 30, 184]. This involves the use of disposable plastic trays sealed with Filmolux Tape. Second, a method of poliovaccine potency testing is described involving inoculation of 3 10-fold dilutions into groups of 15 chicks aged 32–33 days. The chicks are bled 5 days after a 1 ml. injection of the sample. In a routine test 4 vaccine samples are compared with a standard. Third, the method of titrating the sera is described in detail. One dilution, 1/5 of each chick serum, is tested against 6 10-fold dilutions of each virus type. Simultaneously the virus is accurately titrated. The ability of the serum to neutralize virus is shown by a lowering of virus titre. The number of logarithms of virus neutralized is plotted against the dilution of the vaccine sample. Fourth, the use of the method to assess the potency of a type 1 poliovirus sample after gamma irradiation is presented. It is apparent that gamma irradiation in doses of a million rads destroys antigenic potency. The effect on virus titre is not reported. *A. J. Beale*

SMITH, W. **The Immunological Response to Poliomyelitis Viruses. Production of Virus Flocculating and Flocculation-Blocking Antibodies.** *Virology.* New York. 1961, Mar., v. 13, No. 3, 280–87.

SMITH *et al.* [this *Bulletin*, 1960, v. 35, 205] have previously found that the sera of patients convalescent from poliomyelitis or vaccinated with killed poliovaccine usually contain neutralizing, flocculating and complement-fixing antibodies but that there is no correlation between these 3 sorts of antibody. In this paper experiments are described showing that sera containing high titres of neutralizing antibodies but no flocculating antibodies nonetheless block the flocculation of D antigen by potent rabbit flocculating antisera. Such sera are

found in some people vaccinated with killed poliovaccine or in animals (guineapig after 2 doses or British Standard poliovirus antisera made in monkeys.) Flocculation-inhibition was observed by holding virus as crude tissue culture fluid at 37°C. for 2 hours (better results were obtained if this was prolonged for 6 hours) before adding rabbit flocculating serum. Contrary to the experience in man [SMITH *et al., loc. cit.*] flocculating antibodies did not appear in a rabbit until after the peak of neutralizing antibody had passed. All these flocculation and flocculation-inhibition reactions occurred with the D antigen component of poliovirus. Concentrated purified poliovirus antigen was unsatisfactory for blocking experiments, being too strong and partially aggregated [see EGGERS and SABIN, this *Bulletin*, 1961, v. 36, 951]. 2 hypotheses are considered: first, that the 2 antibodies (flocculating and flocculating-blocking or neutralizing) are evoked by 2 type-specific antigen components on the virus surface and, second, that they represent 2 kinds of antibodies directed against 1 antigen. The second idea is favoured. *A. J. Beale*

PERETTS, L. G., BYCHKOVSKAIA, O. V., BAZHEDOMOVA, M. A., BABINA, N. S. & SEMENOVA, N. S. **Effect of Potassium Permanganate on Poliomyelitis Virus.** *Problems of Virology*. London. 1960, v. 5, No. 4, 441–7, [17 refs.] [Translated from Russian.]

Potassium permanganate as a 0·005% solution was found to destroy Theiler's virus after contact for 24 hours and to reduce the titre greatly after 1 minute's exposure. Type 2 poliovirus (Ovchinnikov strain) was introduced into the oseophagus of mice in a dose of about 10^5 [the exact method of titration is not given] and followed by 0·25 ml. of a 0·25% potassium permanganate solution. The titre in HeLa cells of virus in the alimentary canal of treated mice was less than that in controls. Somewhat similar results were found with Theiler's virus in the alimentary canal after treatment with potassium permanganate. It is suggested that this substance should be tried in man in an attempt to prevent poliovirus carriage in the intestinal tract. *A. J. Beale*

CORAGGIO, F., VALOROSO, L., SOLAZZO, G. & GALEOTA, C. Influenza degli steroidi di tipo cortisonico sulla attività citopatogena virale in culture di tessuto. Nota I. Studio dell'effetto del prednisolone sulla attività citopatogena del virus Coxsackie B_2 (ceppo OHIO). **[The Influence of Steroids of the Cortisone Type on the Cytopathic Effects of Viruses in Tissue Culture. I. A Study of the Effect of Prednisolone on the Cytopathic Effect of Type B2 Coxsackie Virus (Ohio Strain)]** *Riv. Istituto Sieroterap. Ital.* 1960, Nov.–Dec., v. 35, No. 6, 627–33. [23 refs.] English summary (8 lines).

The authors have investigated the effect of prednisolone upon the cytopathic effect of type B2 Coxsackie virus. The virus was grown in cultures of a line of human kidney cells. In preliminary experiments the maximum concentration of prednisolone tolerated by the cells was found to be 200 μgm. per cc. When the steroid was added to the cultures after 1 day of growth and dilutions of the virus were added after 4 days the cytopathic effect appeared earlier than in control cultures without steroid, and the titre was 0·5 log unit higher. In similar experiments in which prednisolone was added to the cultures 24 hours before infection and then removed by changing the medium, no difference could be observed in the time of appearance of the cytopathic effect and the titre. When the cells were exposed to the steroid 24 hours before infection and throughout the period of virus growth the appearance of the cytopathic effect was delayed and the titre was 0·7 log unit lower, and when the steroid was added 24 hours after infection the effect was still more marked, with a reduction in titre of 1·3 log units. In titrations of the supernatant fluid of such cultures no reduction in virus content could be observed, and prednisolone therefore prevents the appearance of the cytopathic effect without having any effect upon the multiplication of the virus. *D. J. Bauer*

ROBBA, L. Preparazione di antigeni per la deviazione del complemento nella diagnosi sierologica delle affezioni dovute al gruppo B dei virus Coxsackie, e reazioni crociate nel campo degli enterovirus. **[Preparation of Antigens for the Complement-Fixation Tests in the Diagnosis of Coxsackie Group B Infections and Cross Reactions in Enteroviruses]** *Giorn. di Malattie Infettive e Parassit.* 1961, Feb., v. 13, No. 2, 96–101. [46 refs.]

The point of complement-fixation tests lies in the possibility of discovering antibodies which appear earlier than the neutralizing antibodies. From a group B type 5 Coxsackie virus (Paris Pasteur Institute) 6 antigens were prepared, 2 on newborn mice and 4 on kidney cell and KB cell cultures. For the first, Swiss mice, 1–2 days old, were used, and were killed 4 days after intracerebral inoculation of 0·1 ml. of mouse brain at its second passage. The animals had shown typical symptoms. The brains were extracted by the Casals ether acetone method (antigen I) and the carcasses by the method used at the Pasteur Institute (antigen II). For the second, culture was made (a) on monkey kidney cells in a medium without serum, and (b) on KB cells in a medium containing 2·5% of ox serum. Virus was inoculated in 10 ml. volumes for every 100 ml. of medium, the volume being calculated according to the titre of the virus and the quantity of cells in the culture. When a cytopathic effect had been obtained, the supernatant after centrifugation at 2,500 r.p.m. for 15 minutes was taken and stored at 4°C. (antigens III and V). The centrifuged deposit was resuspended in 5 ml. of sterile buffer solution or in veronal, giving a concentration 20 times that in the original volume. It was then frozen and thawed 6 times, then centrifuged at 2,500 r.p.m. for 15 minutes. The supernatant from the kidney cell culture was antigen IV, that from the KB cells antigen VI. To 0·1 ml. of diluted sera were added 0·1 ml. of antigen I and II diluted at 1/2 and 1/4, of antigens III and V undiluted and at 1/2, and of antigens IV and VI at 1/2 and 1/4 dilution; 0·2 ml. of

complement containing 2 units, and 0·2 ml. of haemolytic system consisting of 0·1 ml. 2% sheep cell suspension and 0·1 ml. of haemolytic serum (3 units). A first trial showed only antigens V and VI to be useful, so the technique was modified by diluting the centrifuged deposit in buffer solution so that its final concentration was 50 times that in its initial volume, the whole being frozen and thawed 8 times.

In a second trial 2 antigens were used: (a) supernatant from KB cell culture undiluted and diluted 1/2, and (b) centrifuged deposit diluted 1/4 and 1/8. These antigens were treated with equal volumes of ether, which was allowed to act for 5 minutes and then separated by centrifuging, the watery part constituting the antigen. Results showed that the antigens so prepared had good type specificity when tested against rabbit sera. While there is no cross reaction between sera of animals immunized with Coxsackie A virus and Coxsackie B antigen, this is partially the case with sera from human cases from whom Coxsackie A virus has been isolated. Similar cross reactions have been noted when sera from human poliomyelitis cases type 1, 2, and 3 have been put up with Coxsackie B antigen though a double infection could not be ruled out. There was no cross reaction between Coxsackie B antigen and sera of animals immunized with ECHO types 3 and 14.

When 5 Coxsackie B antigens were used on 18 human cases of cardiac disease, a satisfactory antibody titre against 1 type was obtained in 3. The author believes the antigen described can be used for diagnostic purposes, bearing in mind the difficulties of estimating antibody titres in the sera of animals suffering from enterovirus infections. *E. Agius*

World Health Organization. Technical Report Ser. No. 219. **Arthropod-Borne Viruses. Report of a Study Group. Geneva, 5–10 September 1960.** 68 pp. [Numerous refs.] 1961. Geneva: Palais des Nations. [Sales agent for U.K., H.M. Stationery Office.] [5s.; $1.00; Sw.fr. 3.–.]

This report of a Study Group reviews procedures for determining the presence, prevalence and importance of arthropod-borne viruses, especially the design of serological surveys and schemes for the isolation of viruses. Classification of arthropod-borne viruses is at present based on serology but when knowledge increases other physico-chemical and biological criteria will have to be considered. The classification is tabulated and the viruses are also classified in terms of vectors and clinical syndromes in man. The methods of assessing the importance of arthropod-borne virus infections in human and domestic animal populations is discussed and it is suggested that cases or outbreaks of infections due to certain agents should be made reportable to WHO and FAO. The principles of ecology of these infections is reviewed and some research problems defined. The creation of a system of reference laboratories and for information exchange including the setting up of a catalogue of arthropod-borne viruses is recommended. Finally control measures are reviewed and special emphasis given to the need for the development of effective and safe vaccines. There is a valuable list of references and also lists of interested entomological and ornithological centres.

C. E. Gordon Smith

Price, W. H., Lee, R. W., III, Gunkel, W. F. & O'Leary, W. **The Virulence of West Nile Virus and TP 21 Virus and their Application to a Group B Arbor Virus Vaccine.** *Amer. J. Trop. Med. & Hyg.* 1961, May, v. 10, No. 3, 403–22. [24 refs.]

The objective of this study was to find a combination of vaccines which would immunize against the whole of group B of arthropod-borne viruses. Two strains of West Nile virus recently isolated from an epidemic in Israel were studied. By intracerebral inoculation of monkeys it was found to be more encephalitogenic than the other and the latter (TL-443) was therefore chosen for further study. It was compared with the Egypt 101 strain: both caused 5–6 days viraemia in chicks and spider monkeys; in rhesus monkeys TL-443 was less encephalitogenic by the intracerebral route. The 2 strains gave similar neutralizing antibody responses in chickens and spider monkeys. With formalinized vaccines tested in mice and chickens TL–443 seemed to give a broader neutralizing antibody response.

Spider monkeys were given 17D virus after which low grade viraemia occurred. 2 months later they, and controls, were given 500 mouse LD50 of TL-443; although they had no West Nile neutralizing antibody, 5 of 10 monkeys inoculated with 17D circulated no West Nile virus and the remainder had a shorter viraemia than controls. Combined vaccination with 17D and TL-443 was found to protect monkeys from viraemia when challenged with Japanese encephalitis virus and almost the same degree of protection was afforded by TL-443 alone.

Spider monkeys were given 100,000 LD50 of 17D followed 2 months later by 3,000 LD50 of TL-443 and 1 month after that one dose of formalinized Russian spring-summer encephalitis (RSS) virus (Moscow strain). 1 month after the 3rd inoculation the monkeys were challenged subcutaneously with 300 LD50 of RSS virus. Only 2 of 6 such monkeys circulated virus briefly compared with longer viraemia in all monkeys given only 17D and West Nile, or given RSS vaccine only although both these had less viraemia than controls. Similar protection as judged by viraemia was demonstrated in similarly vaccinated monkeys against the viruses of Omsk haemorrhagic fever, dengue-3, dengue-4 (haemorrhagic strains), Wesselsbron, St. Louis encephalitis, dengue-1, dengue-2 and Murray Valley encephalitis.

To reduce the neurovirulence of TL-443 it was passaged 10 times in chick-embryos, the central nervous system being removed before grinding up. It was then given 18 passages in chick embryo tissue cultures. Plaque studies were then made and 2 clones were thrice plaque purified. A strain was obtained which was not encephalitogenic in monkeys but circulated as well as the parent strain and was as immunogenic. This attenuation was unaffected by 11 serial intracerebral passages in monkeys with alternate mouse passages or by 6 subcutaneous blood inoculation passages in monkeys. TP21

[Langat] virus [this *Bulletin*, 1957, v. 32, 99], a member of the RSS group caused encephalitis in 2 of 6 monkeys given 20,000 LD50 intracerebrally. After 9 chick embryo and 38 chick embryo tissue culture passages none of 18 monkeys developed encephalitis after 300,000 LD50. These strains caused viraemia not over 1·5 log for 4 days. Triple vaccination was used as above, but adapted TP21 which had been plaque-purified was substituted for the formalinized RSS vaccine. This combination gave marked protection against viraemia in spider monkeys challenged with RSS, Omsk, Central European encephalitis and Kyasanur Forest disease viruses.

C. E. Gordon Smith

KOKERNOT, R. H., MCINTOSH, B. M. & WORTH, C. B. **Ndumu Virus, a Hitherto Unknown Agent, isolated from Culicine Mosquitoes collected in Northern Natal, Union of South Africa.** *Amer. J. Trop. Med. & Hyg.* 1961, May, v. 10, No. 3, 383–6. [12 refs.]

A pool of 19 *Mansonia* (*Mansonioides*) *uniformis* collected at Ndumu in northern Natal in May 1959 was inoculated into newborn mice. On the 6th day all were sick and the brains were passaged to establish a strain pathogenic for adult mice. It was re-isolated. A second strain was isolated from a pool of 278 *Aedes* (*Neomelaniconion*) *circumluteolus* collected 2 days earlier at Ndumu. Re-isolation was unsuccessful. Both strains were filterable through a gradocol membrane of average pore diameter 275 mμ but not through a Seitz EK pad. Cross neutralization and complement-fixation tests showed the strains to be identical. A complement-fixing antigen was tested against antisera to 5 group A, 10 group B and 11 other arthropod-borne viruses but no reaction detected. No haemagglutinin has been prepared but antiserum to Ndumu virus was tested in a haemagglutinin-inhibition test against antigens of 4 group A, 7 group B and 4 other arthropod-borne viruses and no reaction was detected. It was also tested in neutralization tests against antisera to 8 other viruses isolated at Ndumu and 1 other arthropod-borne virus and no reaction detected.

The virus was successfully lyophilized and is sensitive to sodium deoxycholate. It causes encephalitis in mice. After intracerebral inoculation the average survival time in suckling mice is about 3 days and in adults about 7·5 days. In newborn mice intracerebral and intraperitoneal titres were similar but in adults the intraperitoneal titre was 5·5 log lower. It was non-pathogenic for guineapigs but they developed antibody. In a *Cercopithecus* monkey inoculated intracerebrally, viraemia was detected on the 8th and 10th days but no antibody was detected 29 days after inoculation. A booster dose of virus induced antibody formation. Neutralizing antibody to Ndumu virus was found in sera from 5 of 88 children and in 17 of 153 from adults in 8 widely scattered places in southern Africa. *C. E. Gordon Smith*

NICOLAU, S. S. Vaccinuri metalizate (argint, cupru). Nouă metodă pentru prepararea de vaccinuri atenuate contra turbării encefalitei de căpusă, herpesului, gripei si ornitozei. **[Metal-treated Vaccines (Silver, Copper). A New Method of Preparing Attenuated Rabies, Tick-borne Encephalitis, Herpes, Influenza and Ornithosis Vaccines]** *Studii si Cercetari Inframicrobiol.* 1960, v. 11, No. 4, 489–527. [87 refs.] French summary.

[An abstract of this paper appeared in the *Tropical Diseases Bulletin*, 1961, v. 58, 1127.]

ROSEN, L. **Hemagglutination and Hemagglutination-Inhibition with Measles Virus.** *Virology.* New York. 1961, Jan., v. 13, No. 1, 139–41.

The author has found that purified and concentrated preparations of the Edmonston strain of measles virus will agglutinate rhesus red cells. The virus was grown in KB cells, and when the infected cells had fallen off the glass the fluid and cell débris was frozen and thawed and clarified by low-speed centrifugation. Gelatin in a final concentration of 0·06% was added, and the virus was deposited by high-speed centrifugation and resuspended in 1/10 of the original volume. 3 batches of virus prepared in this way agglutinated rhesus red cells to titres of 64–128 at 37°C., and fixed complement to titres of 8–16; the activities were unaffected by heating at 56°C. for 1 hour. The haemagglutinin titres were lower at room temperature and at 4°C. Haemagglutination-inhibition tests were carried out on sera which were first adsorbed with kaolin and then with rhesus red cells. In the examination of sera collected at various times of the illness from 10 children suffering from measles inhibition titres of up to 1,280 were obtained in tests with 4 haemagglutinating units of measles virus, whereas no inhibiting antibody was found in the sera of 7 children known to be susceptible to measles. The results indicate that the haemagglutination-inhibition test is sufficiently sensitive and specific for use as a diagnostic method. *D. J. Bauer*

METTLER, Norma E. Adaptation à l'oeuf du virus de la fièvre hémorragique épidémique de la province de Buenos Aires. **[Adaptation to Eggs of the Virus of Epidemic Haemorrhagic Fever of Buenos Aires]** *C.R. Soc. Biol.* 1960, v. 154, No. 12, 2375.

The virus, adapted to white mice, was inoculated on to hens' eggs (Leghorn) 7–11 days old, at first intra-amniotically and later on to the chorio-allantoic membrane. The eggs were incubated at 36°C. for 5 days, when plaque formation was observed and passage on the membrane was successful.

Convalescent sera, but not sera taken in the acute stage, neutralized the virus. *Charles Wilcocks*

IMMUNITY

GOLDSTEIN, G., SLIZYS, Irene S. & CHASE, M. W. **Studies on Fluorescent Antibody Staining. I. Non-Specific Fluorescence with Fluorescein-Coupled Sheep Anti-Rabbit Globulins.** *J. Exper. Med.* 1961, July 1, v. 114, No. 1, 89–110, 4 text figs. & 3 figs. on pl. [34 refs.]

BORSOS, T. & COOPER, M. **On the Hemolytic Activity of Mouse Complement.** *Proc. Soc. Exper. Biol. & Med.* 1961, May, v. 107, No. 1, 227–32, 4 figs. [13 refs.]

"By use of appropriate intermediates of the complement system, mouse serum has been shown to contain C'1, C'4, C'2 and C'3 complex."

BOE, J. & ØVSTHUS, Ø. **The Properdin System. Serum Properdin Levels in Infectious Diseases.** *Acta Med. Scandinavica.* 1961, Apr., v. 169, No. 4, 423–32, 5 figs. [23 refs.]

Because of the continued interest in the properdi system the authors attempted to determine its value i diagnosis, prognosis and treatment. The serum properdi levels were estimated (by 3 methods in parallel PILLEMER's [this *Bulletin*, 1955, v. 30, 83; 1956, v. 3 598], WILLERS's (*Vox Sang.*, 1959, v. 4, 21) and LEON [this *Bulletin*, 1956, v. 31, 877]) repeatedly throughou the illness of 37 patients. 10 patients had bacteria meningitis, 9 had viral meningitis and meningo-encepha litis, 7 had bacteriaemia due to *Staph. aureus*, and 11 ha pneumococcal pneumonia. In most cases there was n relationship between the properdin titre and the phas of the infection or convalescence. In some the titr remained high throughout the illness; in others, who mad an uneventful recovery, the titre remained low. In a fe cases there was a low titre in the acute phase which ros to normal values in convalescence. On the whole th properdin levels of the group were low, a fact which th authors suggest may be associated with increased sus ceptibility to infection, but they concluded that th properdin system, though interesting from a biologica point of view, was of little or no help in clinica medicine. *D. A. Cannon*

Miscellaneous

MORISON, J. B. & MEDOVY, H. **Smoking Habits of Winnipeg School Children.** *Canadian Med. Ass. J.* 1961, May 6, v. 84, No. 18, 1006–12, 3 figs. [16 refs.]

A short questionnaire was answered (anonymously) by nearly 22,000 Winnipeg schoolchildren. The youngest group approached were children 11-12 years old and though regular smoking among them was very light, even at these ages about 40% of boys and 18% of girls had already smoked their first cigarette. At ages 13–15 25% of boys and 15% of girls were smoking regularly, *i.e.*, one or more cigarettes per week, while at ages 16 and over these figures became 45% and 28%. Where neither parent smoked 21% of the boys and 11% of the girls had smoked in the last 4 weeks. Where one or both parents smoked 28–29% of the boys and 15–20% of the girls had smoked in the last 4 weeks. Smoking was more frequent in classes of below average intelligence and decreased with academic achievement. It is concluded that a programme of smoking education should start by at latest ages 11–15 and be specially directed to boys and to classes of lower academic standing.

Austin Bradford Hill

WEHRLE, P. F., DEFREEST, L., PENHOLLOW, J. & HARRIS, Virginia G. **The Epidemiology of Accidental Poisoning in an Urban Population. III. The Repeater Problem in Accidental Poisoning.** *Pediatrics.* Springfield, Ill. 1961, Apr., v. 27 No. 4, 614–20.

This is the third study of a series on the epidemiolog of accidental poisoning in Syracuse, N.Y. [*Amer. J. Pub Health*, 1960, v. 50, 1705; this *Bulletin*, 1961, v. 36, 508] Its purpose was to analyse the "frequency and character istics of *repeated* episodes of poisoning." 100 childre who had previously been treated at a Syracuse hospita for accidental poisoning were compared in respect o incidence of poisoning in a period of 12 months with th poisoning experience in 100 children with no history o poisoning selected according to age, sex, family size an the socio-economic area in which they lived to matc these characteristics with those of the "poisoned group.

It was found that during a period of 12 months ther were 42 further poisonings in the "poisoned" group whereas only 3 occurred in the control group.

Investigations were made of the behaviour characteris tics of the children, and the family structure. In th poisoned group as compared with the control group ther was "increased motor activity with a tendency to rebe with disciplinary measures" and also "both sexes walke earlier and were more mischievous than was the case o the control group". A further point was "The famil structure associated with poisoning suggests that absenc of father, working mothers, separation experiences an pregnancy may be important factors."

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